

World Journal of *Orthopedics*

World J Orthop 2016 January 18; 7(1): 1-73



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

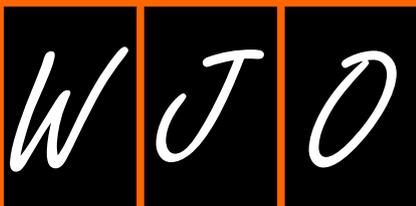
Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*



EDITORIAL

- 1 How to approach the pediatric flatfoot
Vulcano E, Maccario C, Myerson MS

REVIEW

- 8 Football injuries of the ankle: A review of injury mechanisms, diagnosis and management
Walls RJ, Ross KA, Fraser EJ, Hodgkins CW, Smyth NA, Egan CJ, Calder J, Kennedy JG
- 20 Mechanical and cellular processes driving cervical myelopathy
Dolan RT, Butler JS, O'Byrne JM, Poynton AR

MINIREVIEWS

- 30 Role of negative pressure wound therapy in total hip and knee arthroplasty
Siqueira MBP, Ramanathan D, Klika AK, Higuera CA, Barsoum WK
- 38 Direct anterior total hip arthroplasty: Literature review of variations in surgical technique
Connolly KP, Kamath AF
- 44 Total elbow arthroplasty is moving forward: Review on past, present and future
Prkić A, van Bergen CJA, The B, Eygendaal D
- 50 Review of management of unstable elbow fractures
Ozel O, Demircay E
- 55 Calcific tendinitis of the rotator cuff
ElShewy MT

ORIGINAL ARTICLE

Case Control Study

- 61 Patient specific guides for total knee arthroplasty are ready for primetime
Schotanus MGM, Boonen B, Kort NP

CASE REPORT

- 69 Surgical treatment of sacral fractures following lumbosacral arthrodesis: Case report and literature review
Wang Y, Liu XY, Li CD, Yi XD, Yu ZR

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Makoto Makishima, MD, PhD, Professor, Division of Biochemistry, Department of Biomedical Sciences, Nihon University School of Medicine, Tokyo 173-8610, Japan

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed Central, PubMed, Digital Object Identifier, and Directory of Open Access Journals.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Dan Li*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Xue-Mei Gong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 January 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States
Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLICATION DATE
 January 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjnet.com/2218-5836/g_info_20100722172650.htm

ONLINE SUBMISSION
<http://www.wjnet.com/esps/>

How to approach the pediatric flatfoot

Ettore Vulcano, Camilla Maccario, Mark S Myerson

Ettore Vulcano, Camilla Maccario, Mark S Myerson, Institute for Foot and Ankle Reconstruction at Mercy Medical Center, Baltimore, MD 21202, United States

Author contributions: Vulcano E, Maccario C and Myerson MS contributed equally to this work.

Conflict-of-interest statement: The authors and their immediate family declare no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Ettore Vulcano, MD, Institute for Foot and Ankle Reconstruction at Mercy Medical Center, 301 Saint Paul Place, Baltimore, MD 21202, United States. ettorevulcano@hotmail.com
 Telephone: +1-410-3329242

Received: April 7, 2015
 Peer-review started: April 8, 2015
 First decision: July 6, 2015
 Revised: October 19, 2015
 Accepted: November 3, 2015
 Article in press: November 4, 2015
 Published online: January 18, 2016

Abstract

The most difficult aspect regarding treatment of the pediatric flatfoot is understanding who needs surgery, when it is necessary, and what procedure to be done. A thorough history, clinical examination, and imaging should be performed to guide the surgeon through an often complex treatment path. Surgical technique can be divided in three categories: Soft tissue, bony, and arthroereisis. This paper will describe the joint

preserving techniques and their application to treat the pediatric flatfoot deformity.

Key words: Flatfoot; Flexible; Arthroereisis; Pediatric; Planovalgus; Rigid; Pes planus

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This paper discusses the authors' approach to treating the pediatric flatfoot based on their extensive clinical and surgical experience.

Vulcano E, Maccario C, Myerson MS. How to approach the pediatric flatfoot. *World J Orthop* 2016; 7(1): 1-7 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/1.htm>
 DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.1>

INTRODUCTION

Pes planovalgus is a common condition in children. Despite being typically idiopathic, it may be associated with neuromuscular diseases, tarsal coalitions, and the accessory navicular syndrome. A common mistake that is made by surgeons is to consider the pediatric flatfoot as a small version of the adult flatfoot deformity. Indeed, the etiology and management of the deformity may be quite different. Often children are asymptomatic, and the main concern is the foot shape or the parents' concerns for future impairment. The most important challenge for the physician is to distinguish a condition that may have a benign natural history from those that may cause disability if left untreated. The treatment to correct the flat foot deformity can be nonsurgical or surgical. We can divide the surgical techniques used to correct this deformity into three categories: Soft tissue, bony (osteotomies and arthrodesis), and arthroereisis^[1]. It is unlikely that a soft tissue procedure alone can successfully correct the deformity. For such reason

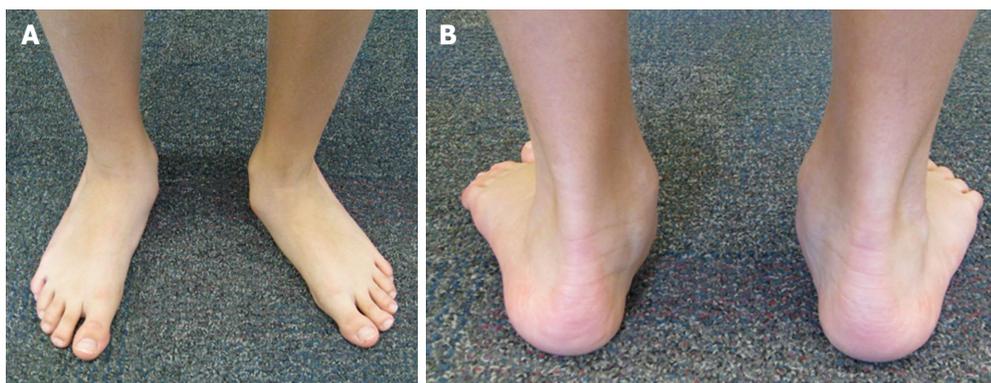


Figure 1 Weightbearing alignment of the foot: Note the left midfoot abduction (A); note the left foot heel valgus and the “too many toes” sign (B).

the addition of bony procedures and/or arthroereisis is warranted^[2]. Subtalar arthroereisis has been introduced in recent years to treat flatfeet in the pediatric population. Arthroereisis is a joint-sparing technique that allows for correction of the deformity through proprioception and mechanical impingement^[3,4].

HISTORY AND EXAMINATION

As crucial as taking a good history is, it may be difficult to obtain information from young patients. They may refuse to cooperate or even minimize their symptoms. In these circumstances feedback from the parents may play an important role. History-taking should include pain, location, intensity, timing, functional problems, and alleviating/aggravating factors. A history of trauma or recurrent ankle sprains should also be specifically questioned^[5].

Patients must be examined both sitting and standing. Flatfoot deformity may be a dynamic deformity that requires weight bearing to be unmasked during clinical examination. The patient must be observed walking barefoot to assess instability and gait asymmetry. It is also important to look at the young patient's shoes to identify asymmetric wear of the soles. When the patient is weightbearing the physician should assess the presence (or absence) of the medial longitudinal arch, the prominence of the navicular, midfoot abduction (*i.e.*, “too-many-toes” sign)^[6], and heel alignment (Figure 1). Children will often present with a hindfoot valgus. Heel rises and manipulation of the calcaneus can confirm flexibility or rigidity of the deformity. A flexible flatfoot is one whose heel valgus can be corrected into neutral or slight varus. Fixed forefoot supination should also be evaluated with manual reduction of the hindfoot deformity, and be addressed in surgical planning by performing a plantar flexion osteotomy of the medial cuneiform.

Finally, Achilles and gastrocnemius contractures must always be identified. As the hindfoot deforms into valgus the Achilles complex is deviated laterally and shortened, leading to contracture that, in turn, aggravates the deformity.

Over time flexible feet in pediatric patients will become more rigid. This may occur in early adolescence or young adulthood. Adaptive changes inevitably take place in the hindfoot that alter its relationship with the forefoot. In order to keep the foot plantigrade, as the hindfoot everts and the calcaneus moves into valgus, the forefoot has to supinate. The Achilles tendon moves laterally with the calcaneus, and the axis of force on the subtalar joint changes, increasing the likelihood of a contracture of the gastrocnemius-soleus. As these structural changes take place, rigidity increases, consequently making the treatment more challenging.

IMAGING

Routine standard radiographs are not essential for diagnosis. However, they should always be ordered to more precisely assess uncharacteristic pain, decreased flexibility, and for surgical planning^[7]. Weight-bearing anteroposterior (AP), lateral, and oblique views of the foot and the ankle should be obtained. Ankle radiographs may demonstrate signs of ankle instability or even overload and compromise of the medial physis. Hindfoot alignment may also be evaluated with Saltzman-view X-rays^[8].

In case of an accessory navicular syndrome, an internal rotation oblique view is recommended in addition to the abovementioned views. A calcaneo-navicular coalition is best seen on the external rotation 45° oblique view, while a talonavicular coalition best visualized on the axial view^[4,9].

The most commonly used radiographic measurement is Meary's angle (or talar-first metatarsal angle): The angle formed by a line through the long axis of the talus and navicular in relation to the first metatarsal axis. A flatfoot demonstrates a negative Meary's angle (apex plantar). On the lateral foot view one can measure the lateral talocalcaneal angle, the talometatarsal angle, and calcaneal pitch. On the AP foot view one can assess the talometatarsal angle and the talonavicular coverage angle^[6].

Computed tomography (CT) scan and magnetic resonance imaging (MRI) are not necessary unless in

patients with uncommon causes of flatfoot deformity^[4].

The CT scan (possible weightbearing) represents the gold standard for the assessment of tarsal coalitions. While many patients with a tarsal coalition show some radiographic evidence (*i.e.*, the "C" sign, talar beaking, or osseous bridging), these may sometimes be absent or unclear on standard X-rays^[6]. Similarly, MRI provides additional information on fibrous coalitions as well as in cases of accessory navicular syndrome where the posterior tibial tendon could be compromised^[5].

TREATMENT

Nonsurgical management

Young patients and their parents should be reassured that most flexible flatfeet are normal in childhood, and that the foot arch elevates over the first 10 years of age^[10]. Although orthotics are diffusely prescribed to alleviate symptoms, to date there is no evidence supporting the use of orthotics to correct the deformity^[11]. As a matter of fact some authors even suggest that insoles could cause more harm, leading to dependency and long-term negative psychological effects^[11-13].

Orthotic supports and bracing may be appropriate for children who are symptomatic, although shoe wear modifications and other inexpensive modalities are quite appropriate for initial management. Custom molded orthotics or custom shoe wear should only be reserved for those that fail the aforementioned modalities. Stretching of a contracted Achilles tendon and physical therapy may offer symptomatic relief as well. The judicious use of nonsteroidal anti-inflammatories is a useful adjunct.

Surgical management

Indications to surgery and the type of surgery to be performed for the pediatric flatfoot continue to represent a challenge for surgeons. Surgical management is recommended in patients complaining of pain and dysfunction. While clinical and radiographic measurements can help stage a deformity, there are no guidelines that help orthopedic surgeons navigate through the different types of surgical procedures. Some patients may present with mild pain but severe deformity, while other may show mild deformity with severe pain.

The techniques available to correct flatfoot deformity can be divided into three procedure categories: Soft tissue, bony (osteotomies and arthrodesis), and arthroereisis.

Soft tissue procedures usually involve the Achilles tendon and/or the gastrocnemius, the posterior tibial tendon, and the peroneal tendons. The aim of these procedures is to balance the deforming forces. A gastrocnemius contracture is almost always present in children with a flatfoot and must be addressed with a gastrocnemius recession. The Silfverskiold test is a useful method to distinguish between a gastrocnemius contracture and an Achilles tendon contracture (the latter requiring a tendo Achilles lengthening, open or

percutaneous). In children, the posterior tibial tendon is typically involved in the accessory navicular syndrome and requires an advancement following a modified Kidner procedure. As for the peroneals, we rarely intervene on them in the pediatric population. Only severe cases of flatfoot deformity with significant midfoot/forefoot abduction could require a peroneus brevis to peroneus longus transfer to allow good realignment and to prevent recurrence.

ARTHROEREISIS

Arthroereisis should only be used to correct hindfoot valgus. Treatment results for children undergoing arthroereisis have been excellent, provided that the talonavicular joint is not significantly uncovered. The procedure seems to work very well in younger children who have predominantly heel valgus, presumably because they have more capacity for remodeling and adaptation of the forefoot. Once the talonavicular joint sags, particularly as seen on the lateral radiographic view, these feet seem to require more correction of the pronation deformity than a medial displacement calcaneal osteotomy can provide. If there is abduction deformity of the foot, with uncovering of the talonavicular joint, then neither the arthroereisis nor the medial displacement osteotomy are likely to be successful. The pediatric patient typically adapts to the arthroereisis very well, and the incidence of implant failure is low in this age-group. By contrast, in our experience with use of arthroereisis as an adjunctive procedure in a group of carefully selected adult patients, sinus tarsi pain warranted implant retrieval in approximately half of the cases. In children, however, implant removal has been necessary in less than 10% of the cases, probably because the foot adapts as it matures.

One cause for failure of the implant regardless of the age of the patient is inadequate correction of the forefoot. When the hindfoot is restored to a neutral position with the implant, some supination of the forefoot occurs. If the forefoot is able to compensate by increased plantar flexion of the first metatarsal, then a plantigrade foot is maintained. If the supination exceeds this adaptive ability, however, then in order to maintain the forefoot in a plantigrade position, the hindfoot has to evert during the foot flat phase of gait. This increased eversion then compresses the subtalar implant, causing pain. For this reason, an opening wedge osteotomy of the medial cuneiform is necessary if supination is excessive.

Intraoperatively, always start with the smallest trial sizes to get a feel for the position, location, and size of the tarsal canal. The range of motion of the subtalar joint should be carefully assessed with each incremental increase in the size of the dilator. The dorsiflexion of the foot now occurs more directly through the ankle joint, rather than in an oblique direction with a combined motion of dorsiflexion and eversion through the subtalar joint. If too large a prosthesis is inserted, motion of the



Figure 2 Weightbearing lateral view X-ray of the left foot prior (A) and post (B) subtalar arthroereisis. Note correction of Meary's angle as well as correction of the hindfoot valgus.

subtalar joint will be limited. An important point here is that the goal of this operation is simply to limit excessive eversion of the hindfoot. If the prosthesis is too small, correction of hindfoot valgus will not be obtained, and dorsiflexion of the foot through the subtalar joint will persist. The appropriate size should limit abnormal subtalar joint eversion and allow for a few degrees of remaining eversion only.

Once the ideal size has been determined, the definitive implant is inserted to rest between the middle and the posterior facets. On the anteroposterior view of the foot, the lateral edge of the prosthesis should be 4 mm medial to the lateral edge of the talar neck.

The range of motion of the subtalar joint, especially eversion with the foot in neutral dorsiflexion, must be reassessed. In most young patients treated for a flexible flatfoot deformity, insertion of the implant is enough to provide appropriate correction (Figure 2). The forefoot should be plantigrade, and no excessive supination of the forefoot should be present after hindfoot correction. If fixed forefoot supination is present, an opening wedge osteotomy of the medial cuneiform is an excellent procedure to correct any residual forefoot supination after correction of the hindfoot.

was first described by Gleich^[14] in 1893. However, it was Koutsogiannis who first recognized that sliding the calcaneus medially improves outcomes in flexible pes planus^[15].

The medial displacement calcaneal osteotomy (MDCO) is a powerful procedure to correct hindfoot valgus. The procedure not only restores the mechanical tripod of the heel with respect to the forefoot, but also medializes the insertion of the Achilles tendon relative to the axis of the subtalar joint^[16,17].

The MDCO requires approximately 10 to 12 mm of translation (about 50% of the calcaneal width). While a dorsal translation must always be avoided, a mild plantar translation of the posterior tuberosity is often desirable to increase the calcaneal pitch angle. Once the displacement has been completed, the choice of fixation is dependent on skeletal maturity. If the physis is closed or reaching skeletal maturity, the construct can be stabilized with one 6.5-mm cannulated screw. If skeletally immature with significant growth remaining, the osteotomy can be stabilized with smooth pin fixation. Once the hindfoot is corrected, attention is turned to the forefoot. Depending on the amount of deformity, additional procedures may be added.

MEDIAL DISPLACEMENT CALCANEAL OSTEOTOMY

The initial concept of mechanically altering the axis or position of the calcaneus to better normalize deformity

CORRECTION OF THE ACCESSORY NAVICULAR SYNDROME

A painful accessory navicular is almost always associated with a flatfoot of variable degree. The symptoms asso-



Figure 3 Postoperative weightbearing anteroposterior (A), lateral (B), and hindfoot (C) views of the left foot in a patient with a painful accessory navicular syndrome treated with a medializing calcaneal osteotomy and fusion of the accessory navicular with a screw. Note correction of the talonavicular uncoverage (A), Meary's line (B), and hindfoot valgus (C).

ciated with this condition result from the disruption of the synchondrosis between the navicular and the accessory bone. As the synchondrosis is stressed, disruption of the attachment of the accessory navicular and thus of the posterior tibial tendon occurs. Another source of pain comes from pressure in the shoe secondary to an uncorrected pronated flatfoot.

Various degrees of deformity and flexibility of the hindfoot are associated with the accessory navicular. A painful accessory bone almost always requires surgical treatment. In addition to addressing the abovementioned condition, additional procedures are often required to correct the foot alignment. Such procedures may include a MDCO, lateral column lengthening, subtalar arthroereisis, medial cuneiform osteotomy, or Achilles tendon lengthening/gastrocnemius recession.

We prefer treating the painful os naviculare with a modified Kidner procedure and advancement of the posterior tibial tendon on the navicular using a suture anchor. However, large accessory bones can be treated with resection of the synchondrosis and fixation with a screw. This has the advantage of preserving the insertion of the posterior tibial tendon on the bone, thus providing quicker recovery and stronger repair (Figure 3). Nonetheless, the disadvantage is the potential for continued swelling on the medial aspect of the foot as well as nonunion. These complications can be decreased by generously shaving both the os naviculare and the medial pole of the navicular, to decrease the bulk of the bone on its medial aspect and expose bleeding subchondral bone.

Intraoperatively, the accessory navicular must be completely excised, taking care not to injure the posterior tibial tendon and the underlying spring ligament. Next, the medial border of the navicular must be resected until flush with the anterior edge of medial cuneiform to decrease the medial bulk. Once the bones have been modeled, the posterior tibial tendon is advanced with the foot in mild overcorrection (plantarflexion and inversion). In young children the tendon can be anchored into the bone using a sharp needle inserted directly into the navicular bone, the cuneiform, or both.

In the older children and adolescents, the use of a suture anchor is preferable. In our experience most patients require additional procedures to correct the foot. These include a gastrocnemius recession, an arthroereisis or a MDCO. These procedures should be done prior to the modified Kidner, as they will affect the tension on the posterior tibial tendon. Conversely, a cotton osteotomy to correct the fixed forefoot supination (often required in our experience) can be performed before or after the modified Kidner.

LATERAL COLUMN LENGTHENING

Sangeorzan *et al.*^[18] presented a cadaveric study in 1993 using the Evans procedure and found significant improvements in talonavicular coverage, talometatarsal angle, and calcaneal pitch angle.

The indications for lengthening of the lateral column (LCL) are quite specific and include a flexible foot that is amenable to correction. In this context, correction implies that the talonavicular joint can be covered with the procedure. The lateral column lengthening procedure does not work well if the foot is stiff.

The hindfoot alignment can be corrected with either a MDCO (to correct the heel valgus) or a lateral column lengthening calcaneus osteotomy. The latter will not only correct the midfoot abduction, but also push the heel medially. A LCL through a calcaneocuboid fusion is not recommended in children.

We make a short incision over the sinus tarsi. The osteotomy is made 1 cm posterior to the calcaneocuboid joint. The position of the osteotomy is marked with a guide pin and checked fluoroscopically. Osteotomy cuts are then made on either side of the guide pin and completed through the neck of the calcaneus. A common mistake is to make the osteotomy too far posterior, causing subtalar impingement. With the osteotomy distracted, the position of the talus relative to the navicular is checked clinically and radiographically, and once positioning is corrected, the appropriate-size auto/allograft is prepared. The size of the graft in children is about 8 to 10 mm on the lateral aspect of the graft, and



Figure 4 Preoperative anteroposterior (A) and lateral (B) views weightbearing X-rays in a child with a flexible flatfoot; on the anteroposterior view, note about 50% of talonavicular uncoverage; postoperative anteroposterior (C) and lateral (D) weightbearing views following a lateral column lengthening and cotton osteotomy. Note the excellent correction of the talonavicular uncoverage (C) and Meary's angle (D).

should be trapezoid shaped as opposed to triangular (Figure 4). Fixation of the graft is not necessary, unless grossly unstable. Potential complications of LCL include lateral foot pain, nonunion, sinus tarsi impingement (typically when the osteotomy is too posterior), and a slight dorsal subluxation of the distal calcaneus (creating prominence of the anterior process of the calcaneus subcutaneously).

OPENING WEDGE OSTEOTOMY OF THE MEDIAL CUNEIFORM (COTTON OSTEOTOMY)

The opening wedge medial cuneiform osteotomy is an excellent adjunct to many hindfoot correction procedures, including lateral column lengthening, MDCO, excision of an accessory navicular, and placement of an arthroereisis implant. Determining the exact indications for this procedure is not easy, because the capacity of the forefoot for plantar flexion subsequent to the calcaneus osteotomy cannot be predicted. As a general rule, if the forefoot is supinated more than 15 degrees, we add a cotton osteotomy.

The incision is made along the dorsal margin of the medial cuneiform. A K-wire is inserted from dorsal to plantar in the middle of the cuneiform, directed slightly proximally. There is a tendency to make the saw cut too vertically and not along the axis of the cuneiform. If this placement is exaggerated, the osteotomy may enter

the metatarsocuneiform joint. The osteotomy should be completed up to the base of the cuneiform without violating the plantar cortex that will act as a hinge. Once the cut is completed, a laminar spreader is inserted into the osteotomy, and as it is distracted, the first metatarsal is plantarflexed, correcting the metatarsal declination angle. A structural bone graft (allograft or autograft) is then carefully tamped into the osteotomy. Contrarily to the LCL graft which should be trapezoid shaped, the cotton osteotomy graft should be triangular. Most times the graft measures between 5 and 7 mm across at the dorsal base of the graft. The osteotomy is very stable once the graft is wedged into place, and fixation is not necessary.

TARSAL COALITIONS

Tarsal coalitions can determine a rigid flatfoot deformity. Historically, coalition resection was indicated for coalitions inferior to 50% of the middle facet, whereas fusion was indicated for coalitions greater than 50%. We disagree with this philosophy and always try to perform a complete resection of any coalition. The decision is guided by the age of the patient, the severity of the deformity, the degree of stiffness, and the presence of arthritis. A CT scan (possibly weightbearing) is always indicated not only to assess the coalition, but also to identify other coalitions which are present in almost 50% of patients. The most common cause of a rigid flatfoot in a child is a talocalcaneal coalition of the

middle facet. The senior author recently presented a new technique to precisely excise the coalition^[19]. A 5-cm incision is created inferior to the posterior tibial tendon, over the coalition. The coalition is identified in the interval between the flexor digitorum longus and flexor hallucis longus. The soft tissue and periosteal flap over the coalition must be elevated away from the coalition to ensure adequate visualization. Next, a 1-cm incision is made over the sinus tarsi soft spot. A guide pin (part of a system for subtalar arthroereisis) is inserted through the tarsal canal and pushed between the coalition and the posterior facet. Then, the coalition is exposed by inserting the arthroereisis sizing device over the guide wire in a lateral to medial direction through the sinus tarsi. The arthroereisis sizer will open up the coalition as it is inserted. In cases of a solid, complete coalition, a fracture occurs along the margins of the coalition. Resection can then be carried out using osteotomes and rongeurs. As the coalition is resected, the sizing guide can be advanced, further opening the subtalar joint and the coalition. With the arthroereisis guide in place, the coalition can be fully resected, allowing visualization of articular cartilage around the resected coalition.

CONCLUSION

Pediatric flat foot deformity should be classified as rigid vs flexible. A combination of soft tissue and bony procedures is almost always necessary to correctly realign the foot and prevent recurrence. Too often surgeons ignore the power of a gastrocnemius recession and a cotton osteotomy when performing reconstructive surgery. A thorough examination of the foot both preoperatively and intraoperatively will help unmask a gastrocnemius contracture and/or a fixed forefoot supination.

REFERENCES

- 1 **Mosca VS.** Flexible flatfoot in children and adolescents. *J Child Orthop* 2010; **4**: 107-121 [PMID: 21455468 DOI: 10.1007/s11832-010-0239-9]
- 2 **Roth S,** Sestan B, Tudor A, Ostojic Z, Sasso A, Durbesic A. Minimally invasive calcaneo-stop method for idiopathic, flexible pes planovalgus in children. *Foot Ankle Int* 2007; **28**: 991-995 [PMID: 17880873]
- 3 **Fernández de Retana P,** Alvarez F, Viladot R. Subtalar arthroereisis in pediatric flatfoot reconstruction. *Foot Ankle Clin* 2010; **15**: 323-335 [PMID: 20534359 DOI: 10.1016/j.fcl.2010.01.001]
- 4 **Uselli FG,** Montrasio UA. The calcaneo-stop procedure. *Foot Ankle Clin* 2012; **17**: 183-194 [PMID: 22541519 DOI: 10.1016/j.fcl.2012.03.001]
- 5 **Dare DM,** Dodwell ER. Pediatric flatfoot: cause, epidemiology, assessment, and treatment. *Curr Opin Pediatr* 2014; **26**: 93-100 [PMID: 24346183 DOI: 10.1097/MOP.0000000000000039]
- 6 **Kwon JY,** Myerson MS. Management of the flexible flat foot in the child: a focus on the use of osteotomies for correction. *Foot Ankle Clin* 2010; **15**: 309-322 [PMID: 20534358 DOI: 10.1016/j.fcl.2010.02.001]
- 7 **De Pellegrin M,** Moharamzadeh D, Strobl WM, Biedermann R, Tschauner C, Wirth T. Subtalar extra-articular screw arthroereisis (SESA) for the treatment of flexible flatfoot in children. *J Child Orthop* 2014; **8**: 479-487
- 8 **Saltzman CL,** el-Khoury GY. The hindfoot alignment view. *Foot Ankle Int* 1995; **16**: 572-576 [PMID: 8563927]
- 9 **Nogarin L.** Retrograde endorthesis. *Ital J Pediatr Orthop* 1997; **13**: 34-39
- 10 **Wenger DR,** Mauldin D, Speck G, Morgan D, Lieber RL. Corrective shoes and inserts as treatment for flexible flatfoot in infants and children. *J Bone Joint Surg Am* 1989; **71**: 800-810 [PMID: 2663868]
- 11 **Helfet AJ.** A new way of treating flat feet in children. *Lancet* 1956; **270**: 262-264 [PMID: 13287124]
- 12 **Rao UB,** Joseph B. The influence of footwear on the prevalence of flat foot. A survey of 2300 children. *J Bone Joint Surg Br* 1992; **74**: 525-527 [PMID: 1624509]
- 13 **Driano AN,** Staheli L, Staheli LT. Psychosocial development and corrective footwear use in childhood. *J Pediatr Orthop* 1998; **18**: 346-349 [PMID: 9600561]
- 14 **Gleich A.** Beitrag zur operative Plattfussbehandlung. *Arch Klin Chir* 1893; **46**: 58-62
- 15 **Koutsogiannis E.** Treatment of mobile flat foot by displacement osteotomy of the calcaneus. *J Bone Joint Surg Br* 1971; **53**: 96-100 [PMID: 5578768]
- 16 **Nyska M,** Parks BG, Chu IT, Myerson MS. The contribution of the medial calcaneal osteotomy to the correction of flatfoot deformities. *Foot Ankle Int* 2001; **22**: 278-282 [PMID: 11354439]
- 17 **Sung IH,** Lee S, Otis JC, Deland JT. Posterior tibial tendon force requirement in early heel rise after calcaneal osteotomies. *Foot Ankle Int* 2002; **23**: 842-849 [PMID: 12356183]
- 18 **Sangeorzan B,** Mosca V, Hansen S. Effect of calcaneal lengthening on relationships among the hindfoot, midfoot, and forefoot. *Foot Ankle* 1993; **14**: 136-141 [PMID: 8491427]
- 19 **Humbyrd CJ,** Myerson MS. Use of a cannulated guide in talocalcaneal coalition resection: technique tip. *Foot Ankle Int* 2015; **36**: 225-228 [PMID: 25237173 DOI: 10.1177/1071100714553468]

P- Reviewer: Graham ME, Kelesidis T

S- Editor: Song XX **L- Editor:** A **E- Editor:** Li D



Football injuries of the ankle: A review of injury mechanisms, diagnosis and management

Raymond J Walls, Keir A Ross, Ethan J Fraser, Christopher W Hodgkins, Niall A Smyth, Christopher J Egan, James Calder, John G Kennedy

Raymond J Walls, Keir A Ross, Ethan J Fraser, Christopher J Egan, John G Kennedy, Department of Foot and Ankle Surgery, Hospital for Special Surgery, New York, NY 10021, United States

Christopher W Hodgkins, Niall A Smyth, University of Miami/Jackson Memorial Hospital, Miami, FL 33143, United States

James Calder, Department of Trauma and Orthopaedic Surgery, Chelsea and Westminster Hospital, London W2 1NY, United Kingdom

Author contributions: Walls RJ was the primary author of the manuscript; Ross KA, Fraser EJ, Hodgkins CW, Smyth NA, Egan CJ and Calder J made the equal contributions to writing and editing of the manuscript; Kennedy JG was the senior author and made critical contributions to the manuscript and provided the final approval.

Conflict-of-interest statement: The authors have no conflicts of interest pertaining to this manuscript. Full conflict of interest statement has been provided for all authors.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Ethan J Fraser, MBBS, Department of Foot and Ankle Surgery, Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, United States. frasere@hss.edu
 Telephone: +1-646-7146617

Received: April 17, 2015

Peer-review started: April 21, 2015

First decision: May 13, 2015

Revised: June 6, 2015

Accepted: September 16, 2015

Article in press: September 18, 2015

Published online: January 18, 2016

Abstract

Football is the most popular sport worldwide and is associated with a high injury rate, most of which are the result of trauma from player contact. Ankle injuries are among the most commonly diagnosed injuries in the game. The result is reduced physical activity and endurance levels, lost game time, and considerable medical cost. Sports medicine professionals must employ the correct diagnostic tools and effective treatments and rehabilitation protocols to minimize the impact of these injuries on the player. This review examines the diagnosis, treatment, and postoperative rehabilitation for common football injuries of the ankle based on the clinical evidence provided in the current literature.

Key words: Management; Soccer; Football; Ankle; Injury

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Injury prevention is paramount in optimizing function and decreasing time lost from sport in footballers. Early recognition of foot and ankle injuries allows implementation of conservative measures aimed at improving function and reducing the risk of re-injury or development of concomitant pathologies. Treatment, whether conservative or surgical, requires an understanding of the mechanical component of injury (*e.g.*, ligament tear, osteophytes), while additionally addressing the biological components affecting healing. This includes restoration of normal proprioceptive pathways through physical therapy programs while also treating the catabolic biochemical environment through

selected use of biological adjuncts including platelet-rich plasma and bone marrow aspirate concentrate.

Walls RJ, Ross KA, Fraser EJ, Hodgkins CW, Smyth NA, Egan CJ, Calder J, Kennedy JG. Football injuries of the ankle: A review of injury mechanisms, diagnosis and management. *World J Orthop* 2016; 7(1): 8-19 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/8.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.8>

INTRODUCTION

Football is the most popular sport in the world, while also being associated with a high injury rate both at professional and amateur levels^[1-3]. Elite soccer players experience between 13 and 35 injuries per 1000 competitive player-hours, with up to 74% resulting from direct player contact. When cause is analyzed, approximately 80% are traumatic in origin and 20% are overuse injuries^[4,5]. The lower limb is most commonly affected with the ankle accounting for up to a third of all injuries^[1-3,6]. At the 2004 Olympics, foot and ankle injuries were encountered in football proportionally more than any other team sport^[7]. During the 2010 FIFA world cup, ankle sprains were among the most prevalent diagnoses and of these, approximately 50% prevented participation in training or competition^[8]. Additionally a recent study of an English Premier League (EPL) club revealed over a four year period, 20% of injuries were of the foot and ankle with a resultant mean return to sport time of 54 d^[9].

The consequences of ankle injuries include reduced physical activity and endurance levels, lost game time, and considerable medical cost^[3,10,11]. Due to the frequency and debilitating nature of these injuries it is critical for trainers, therapists, and team physicians to correctly diagnose injuries as early as possible and apply the most effective treatments to return athletes to the field expeditiously.

This article reviews the mechanisms of injury and highlights appropriate examination, diagnostics, treatment, and postoperative rehabilitation for common soccer injuries of the ankle.

ANKLE SPRAINS AND ANKLE INSTABILITY

Ankle sprains are the most common pathology accounting for up to 67% of all soccer related ankle injuries^[12,13]. Analyzing ankle sprains in players from the English football league over a 2-year period, Woods *et al.*^[13] found the majority were sustained during player contact (59%) except for goalkeepers in whom 79% occurred during non-contact situations. In addition, Jain *et al.*^[9] showed a 28.6% recurrence in anterior talofibular ligament (ATFL) injury in their EPL cohort. In a typical sprain, forced ankle

inversion-supination precipitates tearing of the ATFL to varying degrees. Video analysis of ankle injuries in professional soccer players has shown that direct contact with a laterally directed force on the medial aspect of the lower leg just before or at foot strike can cause the player to land with the ankle in this vulnerable inverted position^[14]. The injury tends to be more severe if the affected foot is planted and weight-bearing at the time of impact^[6]. The peroneal tendons are also at risk in a combination of mechanical stretch and overload as they attempt to evert the foot back into neutral alignment.

Mechanical instability occurs when ligaments fail to remodel to normal length, allowing motion beyond normal physiological limits. The ankle joint capsule and soft tissues about the joint are often stretched or torn at the time of injury, disrupting the proprioceptive nerve fibers that run through them. This can produce a functional instability where the player may be mechanically stable but unable to maintain balance when in unilateral foot stance^[15]. Both mechanical and functional instability may be present independently or in combination in any player and if untreated can potentiate additional sprains and the development of chronic ankle instability^[16].

Clinical examination may be difficult in the immediate period following an acute injury. If there is concern for a ligamentous ankle injury, consideration can be given to delaying a definitive examination for up to 5 d in the off season as this permits the partial resolution of swelling and inflammation. van Dijk *et al.*^[17] have reported a diagnostic sensitivity of 96% with a delayed assessment protocol. The anterior drawer and valgus stress test can be useful in the delayed or chronic setting, however, these tests have been shown to have limited sensitivity and significant variability in differing examiners hands^[18]. The modified Romberg test can demonstrate proprioceptive deficiencies of the ankle, indicating the presence of functional instability^[19].

During the active playing season consideration should be given for early and accurate diagnosis. Clinical diagnosis will direct further diagnostic tests including plain radiographs, magnetic resonance imaging (MRI) and computed tomography (CT). Ankle sprain is not a benign injury and up to 75% of these injuries will have an associated soft tissue pathology^[20]. MRI has the sensitivity required to detect these associated injuries including osteochondral lesions (OCL's), tendinous and syndesmotic tears, and associated fractures. Plain radiographs may miss up to 50% of OCL's of the talus following ankle sprain and CT scan, while useful in evaluating bony injury, lacks the sensitivity for diagnosis of soft tissue pathology^[21].

Specific clinical tests can direct the radiographic diagnostic intervention. The so called "high ankle sprain" or syndesmotic injury is typically identified by pain over the anterior inferior tibiofibular ligament (AITFL) and interosseous membrane. More specific and sensitive evaluations are the squeeze test of the mid-fibula and resisted external rotation test respectively^[22,23].



Figure 1 Plain radiographs of the left (A) and right (B) ankles of a single patient in the coronal plane. Both ankles are under eversion stress. The right ankle was symptomatic. Only subtle syndesmotic gapping and widening of the medial clear space can be appreciated on the right compared to the left ankle.

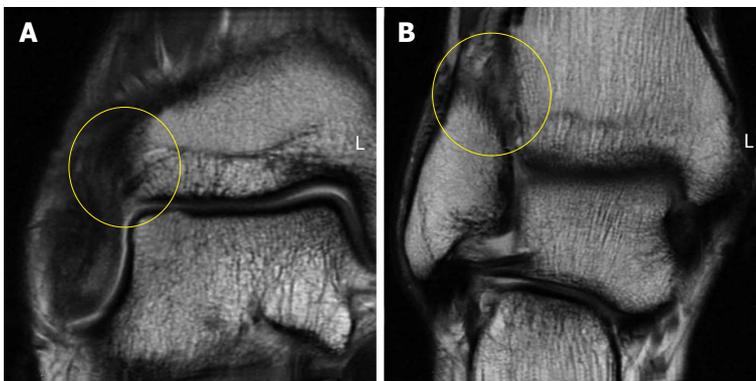


Figure 2 Coronal fast-spin echo proton density magnetic resonance images of the right ankle seen in Figure 1. Disruption and remodeling of the anterior inferior tibiofibular ligament (A; yellow circle) and interosseous ligament (B; yellow circle) can be appreciated.



Figure 3 Axial fast-spin echo proton density magnetic resonance images of the right ankle seen in Figures 1 and 2. Disruption and remodeling of the anterior inferior tibiofibular ligament (yellow arrow) can be appreciated.

Augmenting clinical assessment and subtle injuries diagnosed by plain radiograph with MRI is recommended to fully evaluate the injury with a reported accuracy of 97% (sensitivity: 100%; specificity: 97%) (Figures 1-3)^[22,24].

The peroneal tendons are injured in up to 25% of acute ankle sprains acting as secondary stabilizers^[20]. Resisted eversion is useful to assess the integrity of the peroneal tendons^[25]. MRI is again useful in detecting

any peroneal pathology and dynamic ultrasound can be a useful adjunct in detecting subtle peroneal injury^[26,27].

The so called "low ankle sprain" or pain in the sinus tarsi secondary to a torn interosseous ligament in the acute phase and scar formation in the chronic phase can be examined by direct local pressure in the sinus tarsi while inverting the mid-tarsal joint. Radiographic evaluation including MRI and ultrasound are often less sensitive and specific for the low ankle sprain than for other ankle pathology and a small local anesthetic injection to the area can often be helpful in elucidating the source of pain.

The majority of simple ankle sprains heal with non-operative treatment, however, there is no consensus on the ideal rehabilitation protocol^[20]. Early mobilization followed by phased rehabilitation is advocated by most authors as beneficial in minimizing time lost^[28-30]. A multicentre study of 584 patients suggested there is faster recovery with a short period of immobilization in a below the knee cast or removable boot when compared to treatment in a compression bandage^[31]. It must be noted that no information was provided on additional interventions, the study utilized a postal questionnaire and there was a 17% drop-out rate. But overall, the results indicate initial immobilization can be beneficial. Conversely, prolonged immobilization of greater than 2

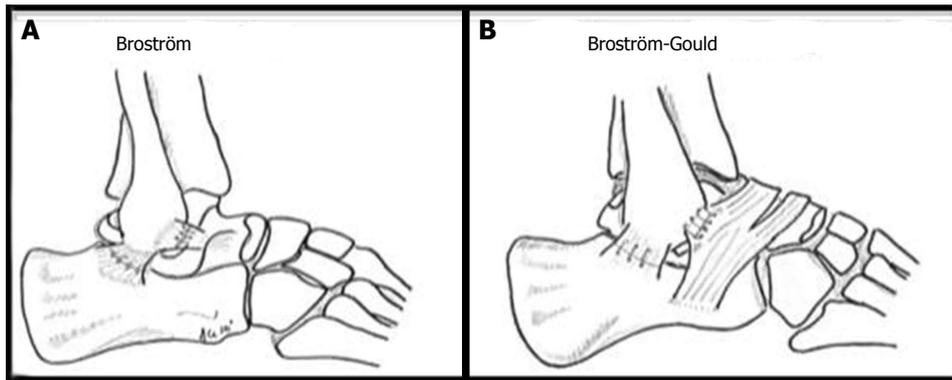


Figure 4 Illustrations of the Brostrom (A) and Modified Brostrom-Gould (B) surgical technique for lateral ligament reconstruction of the ankle. Reproduced, with permission, from Prisk *et al.*^[108].

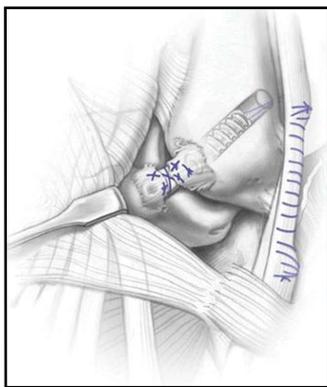


Figure 5 Illustration of the hybrid anatomic lateral ligament reconstruction^[27]. A tendon autograft taken from the peroneus longus has been docked in the talus and distal fibula and remaining anterior talofibular ligament fibers have been sutured over the reconstruction, theoretically allowing proprioceptive fibers to aid in regaining functional stability. Illustration copyright of and reproduced with permission from Kennedy JG, MD. Reproduction without express written consent is prohibited. Reproduced, with permission, from Kennedy *et al.*^[40].

wk has a detrimental effect on muscles, ligaments, and joint surfaces and may result in longer return to play time^[32].

A rehabilitation protocol should be divided into specific stages: Acute and subacute pain and swelling control; range of motion and strengthening exercises; soccer specific functional training; and prophylactic intervention with balance and proprioception stimulating exercises. Upon return to play, continued proprioceptive training is vital to minimize recurrence^[33-36]. Semi-rigid orthoses and air-cast braces may help prevent ankle sprains, especially in athletes with a history of recurrent instability^[37-39]. Bracing has a mechanical advantage over simple taping, as tape loses its ability to restrict inversion and eversion approximately 20 min after starting activity^[39].

Surgery is indicated in patients with chronic mechanical instability. Traditionally, two forms of repair are considered: An anatomic reconstruction such as the Brostrom or Gould modification (Figure 4), or a non-anatomic checkrein tenodesis such as the Chrisman-

Snook procedure^[20,40]. Anatomical repairs appear to produce better outcomes and there is additional concern that some checkrein procedures can restrict subtalar motion and prevent normal agility on playing surfaces by altering hindfoot biomechanics^[38,41-43]. As over 90% of patients with chronic ankle instability have additional intra-articular lesions, arthroscopic ankle evaluation, and treatment where necessary, can be performed at the same time as open lateral ankle ligament repair^[44,45].

With acute ankle ligament instability the traditional treatment paradigm of triple phase physical therapy and avoiding surgical intervention has been recently questioned. A report from van Dijk demonstrated superior results with acute surgical repair in a cohort of athletes^[46]. It consisted of a subgroup analysis in which only a single surgeon series of acute operative repair was conducted. Objective instability, as defined by a positive talar tilt on stress radiographs or positive anterior drawer sign, was significantly less when compared to non-operative treatment. Because increased objective instability is a predictor for future ankle sprains, an acute reconstruction may be preferred in professional athletes^[47,48]. The outcome of a recent consensus meeting also suggested a role for selective operative treatment in athletic populations^[43].

Surgical outcomes in acute and chronic lateral ankle ligament repairs are generally good and most athletes are able to return to their pre-injury level of function^[20]. Kennedy *et al.*^[40] reported an anatomic repair augmented with a portion of peroneus longus used as an ATFL checkrein in 57 athletes, including 11 soccer players (Figure 5). Although all patients achieved mechanical stability, five patients did not return to their pre-injury level for reasons unrelated to their ankle. Maffulli *et al.*^[49] recently reported outcomes of ankle arthroscopy and Brostrom repair in 38 athletes at an average 8.7 years follow-up. Laxity grade, American Orthopaedic Foot and Ankle Society Ankle-Hindfoot scores, and Kaikkonen scales all improved significantly at last follow up. Return to high contact sport was allowed six months postoperatively. Fifty-eight percent of patients returned to their pre-injury level of activity, 16% decreased their



Figure 6 Coronal fast-spin echo proton density magnetic resonance image demonstrating an uncontained osteochondral lesion of the medial talar dome.

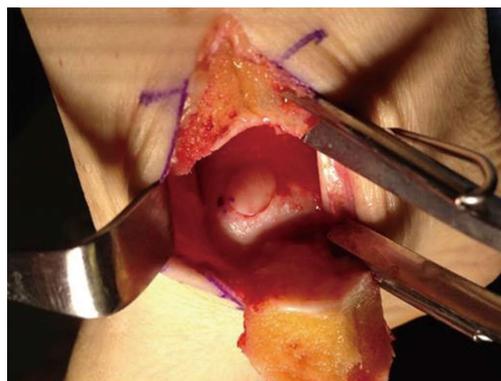


Figure 7 Intraoperative photograph of an autologous osteochondral graft transplanted into the medial talar dome. Access was achieved via a medial malleolar osteotomy. The graft was gently tamped into position until flush with the surrounding surface.

activity but maintained activity in less demanding sports, and 26% abandoned sport participation but remained physically active. Arthroscopic assisted techniques are emerging and may play a role in some cases, but its exact role has yet to be determined and open techniques are currently considered the gold standard^[50].

Acute syndesmotic injuries (high ankle sprains) are less common than lateral ankle sprains and if missed can potentiate persistent morbidity and early degeneration of the ankle joint^[51,52]. Mild syndesmotic sprains can be managed conservatively with protected weight-bearing and functional rehabilitation. Compared with lateral ankle sprains, syndesmosis injuries typically require longer rehabilitation programs^[52]. A recent study of National Football League players, however, did indicate an earlier return to play (4-6 wk) is possible with milder injuries^[53]. Due to the potential for prolonged rehabilitation, some clinicians advocate surgical intervention in professional athletes with mild sprains to expedite a return to play^[52].

Surgical intervention is necessary in severe acute injuries where there is tibio-fibular diastasis. Screw fixation has traditionally been utilized with most physicians advocating screw removal between 7 and 12 wk postoperatively^[51,52]. Non-absorbable suture-button fixation devices have more recently emerged as a fixation technique^[54]. They have the advantage of obviating hardware removal and can allow earlier weightbearing^[55]. Chronic syndesmotic injuries can be treated with screw fixation, arthrodesis and arthroscopic debridement. While there are no papers specifically assessing outcomes in an athletic populations, a recent systematic review and meta-analysis reported screw fixation as the most successful treatment option^[51].

OCL's

OCL's of the ankle have an incidence between 50% and 70% of all acute ankle sprains and fractures^[56-59]. Unfortunately, cartilage injuries have a poor spontaneous healing response. Therefore the role of surgical management involves the repair an acute lesion when possible, initiating fibrocartilage formation with

marrow stimulation techniques in small lesions, with consideration given to cartilage transplant or other modalities for larger lesions. The ultimate aim is to return the athlete to their pre-injury level of play.

Symptoms of an OCL may be mechanical and include clicking or locking of the ankle. Typically however, talar OCL's present localized deep joint pain without any mechanical symptoms. Physical examination may reveal swelling, localized tenderness along the joint line, and limited motion. Plain radiographs may miss up to 50% of OCL's and CT is only useful in obtaining the degree of bone injury as both are unable to assess overlying cartilage^[21,60]. Magnetic resonance imaging is recommended for a definitive diagnosis and T2 Mapping sequences can be useful with increased sensitivity to cartilage change (Figure 6)^[61].

Lesion size and location determine the most appropriate treatment strategy. Most OCL's will not heal with conservative treatment and therefore surgery is typically recommended^[62]. Reparative surgical techniques such as bone marrow stimulation for lesions of less than 15 mm in diameter yield good functional outcomes in short term follow-up^[56,63]. Larger lesions are best treated with replacement strategies including autologous osteochondral transplantation (AOT) (Figure 7) or other techniques including autologous chondrocyte implantation^[64-66].

Both reparative and replacement strategies have been evaluated in regards to return to soccer however the evidence is limited in both groups. Saxena and Eakin^[57] evaluated functional activity after surgical management of OCL's in 44 athletic subjects of which 18 were considered high level, including six soccer players. At medium term follow-up (32 mo), 17 of 18 high level athletes had returned to their pre-injury level and the other subject had not returned for personal reasons. The mean time to return to sport was 15 wk after marrow stimulation and 19 wk after bone grafting (not AOT's). More recently, Paul *et al.*^[64] assessed sports activity after talar AOT's in 131 patients with a mean age of 31 years. Seventy percent were either very satisfied or satisfied

by the procedure and 85% required no analgesia when currently involved in sports. While 20% were involved in competitive sports preoperatively, only half of these were still competing postoperatively. Age at time of injury may be a factor in a person's ability to return to sport. For example, Hangody *et al.*^[65] reported a combination of talar and knee OCL's in 354 competitive athletes including 67 soccer players and four Olympians. They found that 63% were able to return to their same activity/sporting level although most were under the age of 30 years. Overall, 9% had to give up sports completely.

The long-term outcome of cartilage repair surgeries has prompted significant interest in biologic augmentation of cartilage healing in the sports world. Concentrated bone-marrow aspirated (CBMA), typically obtained from the players iliac crest at the time of surgery, is a source of mesenchymal stem cells and growth factors. This can be delivered directly to the OCL during arthroscopy and may potentially enhance the healing environment. When combined with microfracture in a large animal model, the resultant cartilage of the CBMA group demonstrated greater type-II collagen, proteoglycan and glycosaminoglycan content consistent with a more normal cartilaginous architecture^[67]. At this time no long term data exists to support the use of CBMA and early return to sport following talar OCL surgery.

Platelet-rich plasma (PRP) is an autologous blood product that contains many growth factors that may promote cartilage repair. A recent review of PRP basic science literature found that it promotes chondrocyte and mesenchymal stem cell proliferation, type II collagen deposition, and proteoglycan deposition^[68]. Results also indicated that PRP may increase chondrocyte viability, promote migration and chondrogenic differentiation of mesenchymal stem cells, as well as inhibit the effects of inflammatory cytokines. Mei-Dan *et al.*^[69] recently compared intra-articular injections of PRP and hyaluronic acid (HA) for non-operative management of talar OCL's in a randomized trial of 30 patients. Fifteen patients were randomized into each group, treated with three consecutive injections of either PRP or HA, and followed for 28 wk. American Orthopaedic Foot and Ankle Society Ankle-Hindfoot scores, visual analogue scale (VAS) pain, VAS stiffness, VAS function, and subjective global function scores all improved significantly more in the PRP group than the HA group. Current clinical studies are limited for PRP, and formal randomized human trials are required to determine the true *in-vivo* effect.

Postoperative care is dependent on the chosen treatment. After marrow stimulation, the patient is initially non-weight-bearing in a soft leg cast for two weeks during which ankle pump exercises are performed three times daily. At two weeks, the patient is placed in a CAM boot and encouraged to start range of motion exercises. At six weeks, patients commence weight-bearing starting with 10% of their body weight, increasing by 10% daily

until full weight-bearing is achieved. Formal rehabilitation concentrates on balance, joint proprioception, and stabilization. Strengthening and sport specific exercises begin at 10 wk. After an AOT procedure, patients are non-weightbearing for six weeks followed by two weeks of progressive weight-bearing as above. At eight weeks, formal physical therapy commences and sport-specific training introduced at 12 wk. Return to soccer is typically at six months following surgery.

ANTEROLATERAL IMPINGEMENT

Anterolateral impingement syndrome (ALI) typically manifests as chronic anterolateral ankle pain following an ankle sprain. It is thought to result from the entrapment of hypertrophic soft tissues or torn and inflamed ligaments in the lateral gutter and anterolateral ankle joint^[70]. Following tears of the ATFL, AITFL, and/or CFL, repetitive motion after incomplete healing can lead to inflammation and subsequent synovitis with scar tissue formation^[71]. Mild sprains with minimal capsular tearing may also produce an intraarticular hematoma, the reabsorption of which by synovium in the lateral gutter may induce a reactive synovitis^[71,72].

Players typically present with chronic ankle pain, limited dorsiflexion, and swelling after activity^[73,74]. Tenderness on palpation of the anterolateral gutter is characteristic. ALI can be distinguished from antero-medial impingement (AMI) if pain is elicited on palpation lateral to peroneus tertius^[74,75]. Symptoms must also be differentiated from sinus tarsi syndrome and a diagnostic injection of local anesthetic is useful in deducing this.

While standard radiographs are effective in diagnosing the presence of anterolateral osteophytes, MRI can reveal soft tissue impingement^[74-76]. However, as false-negative results have been reported with MRI, arthroscopy is generally advocated as the definitive diagnostic and therapeutic modality^[71,77].

Initial treatment involves physical therapy modalities with deep tissue massage and other techniques to reduce inflammation. If after one month of therapy no improvement is noted an ultrasound guided injection to the soft tissue impingement with a combination of low dose steroid and local anesthetic may be useful. Surgical treatment is reserved for recalcitrant cases. During the playing season players can be treated with conservative modalities and surgery may be delayed until the off season. Surgical management includes arthroscopic excision of a pathologic fascicle of the ATFL if present as well as hypertrophic synovium in the lateral gutter (Figure 8). At the end of the procedure range of motion of the ankle is checked under direct arthroscopic visualization to ensure no impingement remains during full dorsiflexion^[71].

Following surgery, the player should remain non-weightbearing for two days. Dorsi- and plantarflexion exercises should commence one day postoperatively to minimize arthrofibrosis. Weight bearing is increased as tolerated. Physical therapy begins after one week and

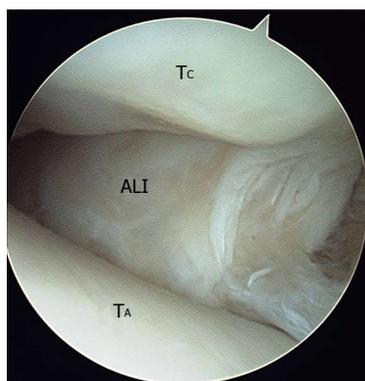


Figure 8 Arthroscopic image of soft tissue impingement the later gutter of the ankle joint. ALI: Anterolateral soft tissue impingement including cicatrized tissue, entrapped lateral ligaments, and hypertrophied synovium; TA: Talar dome; Tc: Tibial cartilage.

soccer-specific training is recommended at 2-3 wk.

There is no published outcome data in a soccer-specific cohort following surgical management for anterolateral ankle impingement; however, reported outcomes in general athletic populations are considered very good^[78,79]. In a series of 11 elite dancers, Nihal *et al*^[80] reported postoperative improvement in all performers with 9 returning to full function at a mean of 7 wk. DeBerardino *et al*^[79] reported a series of 60 athletes with chronic anterolateral soft-tissue impingement following ankle inversion trauma treated with arthroscopic debridement. At a mean of 27 mo follow-up, 85% of patients had an excellent outcome on the West Point Ankle Score. Average functional results of the 12 m single-leg hop test was 94% of the time obtained compared to the unaffected side. Eighty-three percent of patients experienced good to excellent subjective pain relief.

ANTEROMEDIAL IMPINGEMENT

First termed footballer's ankle by McMurray^[81] in 1950, AMI is a common cause of ankle pain in soccer players. This is generally a bony rather than soft-tissue impingement and causative factors include direct trauma, recurrent microtrauma, and chronic ankle instability^[73,81-83].

Recurrent stressing of the ankle at the extremes of motion was previously thought to induce bone spur formation and soft tissue proliferation due to traction of the capsule^[74,75]. Current thoughts on the actual pathogenesis are less clear. Cadaveric analysis has found the anterior joint capsule to be attached more proximally than the site of the tibial spur, and arthroscopic evaluation generally identifies the osteophytes to lie within the joint capsule^[84-86]. Microtrauma from recurrent impact of a football on the anterior ankle may also contribute to osteophyte formation^[82]. Thickened soft tissue can be compressed between talar and tibial osteophytes (kissing lesions) with ankle dorsiflexion causing focal inflammation and pain^[75,85].

AMI commonly presents as anteromedial ankle pain, swelling after activity, and sometimes limited dorsiflexion^[73]. Tenderness with palpation medial to the tibialis anterior tendon is considered indicative of AMI^[75]. Forced hyperdorsiflexion does not always provoke the players typical pain^[75].

The diagnosis of AMI is usually confirmed by plain film radiology^[87]. Anterior tibial osteophytes can be seen with standard lateral views. An oblique AMI view (45° craniocaudal, 30° external rotation of the leg with the ankle in full plantarflexion) is recommended when plain radiographs are negative as it can provide specific visualization of anteromedial osteophytes (Figure 9)^[75]. CT may aid in confirming the diagnosis and MRI can identify soft-tissue impingement, soft tissue injuries, or OCL's^[76].

Ultrasound-guided corticosteroid injections can reduce the patients symptoms temporarily, however, definitive treatment is typically achieved surgically^[84]. This is in contrast to ALI which will often respond to conservative therapy. Operative treatment involves removal of any cicatrized soft tissue and synovial hyperplasia from the joint capsule and a thorough osseous resection of the anterior distal tibia and talar neck. Careful resection to the anterior border of the medial malleolus is vital. Range of motion assessment under arthroscopic visualization is advised to confirm an adequate debridement. The postoperative treatment course is the same as previously described for ALI.

The largest reported series for surgical management of AMI involved 41 patients of which 16 were active soccer players and one retired professional player^[88]. Overall, 93% were satisfied with their outcome. For the athletic population, return to play was 7 wk on average, with longer recovery times in those that required additional procedures, specifically lateral ligament reconstruction (15 wk) and microfracture for OCL's (14 wk). All but one of the athletic cohort (33 of 34 patients) returned to their same level of play indicating an expectation of return to play following this procedure^[40].

POSTERIOR ANKLE IMPINGEMENT

Posterior ankle impingement (PAI) is characterized by posterior ankle pain with plantarflexion. Causative pathologies include a prominent posterior talar process (os trigonum), fracture of the lateral tubercle of the posterior talar process, compression of posterior soft tissues, traction on the posterior talofibular ligament (PTFL) and posterior capsule, and flexor hallucis longus (FHL) tendonitis or tenosynovitis. Repetitive plantarflexion, as seen with ball striking, can precipitate overuse injury^[89-91].

Pain from ankle hyperplantarflexion is due to compression of the soft tissue or bony structures between the posterior aspect of the distal tibia and the calcaneus. Zwiers *et al*^[75] described a simple clinical test where rapid passive hyperflexion of the ankle was combined with a rotational grinding motion at maximal plantarflexion.



Figure 9 Standard lateral views about anterior tibial osteophytes. Lateral plain radiograph of a right ankle with clinical suspicion of anteromedial impingement (A). An anteromedial radiographic view with 30 degrees of external rotation of the same ankle demonstrated an osteophyte on the anteromedial aspect of the distal tibia (B) that could not be appreciated on the lateral view.



Figure 10 Lateral plain radiograph of a right ankle revealing an os trigonum, which was clinically symptomatic, as well as anterior tibial and talar osteophytes.

They found a negative test could exclude PAI. Injection of local anesthetic can further aid in confirming the diagnosis.

Maximal ankle dorsiflexion can also reproduce pain due to tension within the posterior joint capsule and PTFL. Depending on the exact underlying pathology, pain can be elicited with focal palpation of the PTFL, transverse tibiofibular ligament, posterior inferior tibiofibular ligament (PITFL), CFL within the posterolateral gutter, or FHL.

Plain film radiology can help confirm PAI. The lateral ankle view is most useful in detecting osteophytes, calcifications, loose bodies, chondromatosis, and retrocalcaneal bursitis (Kager's triangle) (Figure 10). To differentiate between a hypertrophied posterolateral talar process and an os trigonum, a lateral radiograph with the foot in 25° of external rotation in relation to the standard lateral radiograph is useful^[75]. Further assessment with MRI may identify associated flexor tendon injury, most commonly FHL^[92,93].

Conservative treatment is initially recommended for most patients with additional consideration given to ultrasound-guided corticosteroid injections for more severe cases^[94]. Surgery can be offered for recalcitrant conditions. If bone impingement is determined as

the underlying cause, we advise a single diagnostic injection of local anesthesia and caution against multiple injections as they are ultimately associated with prolonged postoperative recovery^[95]. Elite soccer players require prompt return to play, and surgery should be considered early in the treatment algorithm^[96,97].

While arthroscopic procedures can permit earlier rehabilitation than traditional open procedures there is concern regarding the potential risk of neurovascular injury. Several studies have shown that the rate of nerve injury in patients treated with posterior ankle arthroscopy is lower than that found in anterior arthroscopy as long as care is taken to avoid structures medial to the FHL tendon^[97-99].

Following posterior ankle arthroscopy players remain non-weightbearing in a compression bandage for 24-28 h. Weight bearing is subsequently increased as tolerated until full-weight bearing by one week^[95,100]. Early range-of-motion exercises help prevent cicatrization and stiffness. Physiotherapy is focused on restoring strength and range of motion.

A recent current concepts review illustrates the technique for posterior ankle arthroscopy and management of posterior impingement and co-existing pathologies^[98]. As for anterior impingement syndromes, arthroscopic treatment is very effective at restoring an athlete's ability to return to competitive sport with a very low incidence of postoperative complications^[95,96,99,100]. Calder *et al*^[95] reported on hindfoot arthroscopy for 27 professional soccer players experiencing bone and/or soft tissue impingement. Overall, the mean time to return to training was 34 d and return to playing was 41 d. Recovery, measured as return to training, was faster in cases of soft tissue impingement (mean, 28 d) compared with osseous injury (mean, 40 d). The authors reported only one non major complication of portal leakage which resolved with two weeks rest^[95].

CONCLUSION

Preventing injuries and minimizing lost playtime is the main goal for physicians and trainers and can be

achieved *via* accurate diagnosis, effective treatment, and proper rehabilitation or postoperative course.

While most injuries in soccer occur as a result of player-to-player contact, a significant number of non-contact injuries also occur. The risk of suffering from non-contact lower extremity injuries may be lowered by implementing in-season neuromuscular training programs aimed at enhancing ankle and knee proprioception. Effective warm-up programs with an emphasis on stretching, regular cool down at the end of training or competition, sufficient recovery and rehabilitation programs, proper equipment, and good field conditions can all contribute to injury prevention^[9].

Cleated shoe wear provides traction on the field while running and cutting but high shoe-surface traction has been suggested as a culprit for many ankle injuries. Longer cleats should be avoided due to the increased shoe-surface traction^[101,102]. There are inherent advantages and disadvantages to both natural grass and artificial turf. Higher frictional resistance and shoe-surface traction, which is the case in turf fields, correlates with increased performance, but also increases the incidence of injuries^[103]. Artificial turf also increases plantar pressures, potentially mediating metatarsalgia and stress fractures^[104,105]. Natural grass has a lower friction coefficient than artificial turf but certain species are associated with increased risk of injury^[106]. Warm conditions also harden the ground, resulting in increased shoe-surface traction and risk of injury^[106]. Preventive measures including selecting appropriate cleats length and softening the field through watering should be considered.

Age and gender represent important risk factors for soccer players^[107]. As players age, they should devote more time to appropriate warm-up, stretching and strengthening routines in order to prevent injury. Adhering to a well-designed training program throughout the season and treating injuries promptly and adequately will allow the soccer player to make the most out of the season and minimize lost play time.

REFERENCES

- 1 **Arnason A**, Sigurdsson SB, Gudmundsson A, Holme I, Engbreten L, Bahr R. Physical fitness, injuries, and team performance in soccer. *Med Sci Sports Exerc* 2004; **36**: 278-285 [PMID: 14767251 DOI: 10.1249/01.MSS.0000113478.92945.CA]
- 2 **Junge A**, Dvorak J, Graf-Baumann T, Peterson L. Football injuries during FIFA tournaments and the Olympic Games, 1998-2001: development and implementation of an injury-reporting system. *Am J Sports Med* 2004; **32**: 80S-89S [PMID: 14754863 DOI: 10.1177/0363546503262283]
- 3 **Wong P**, Hong Y. Soccer injury in the lower extremities. *Br J Sports Med* 2005; **39**: 473-482 [PMID: 16046325 DOI: 10.1136/bjism.2004.015511]
- 4 **Dvorak J**, Junge A. Football injuries and physical symptoms. A review of the literature. *Am J Sports Med* 2000; **28**: S3-S9 [PMID: 11032101]
- 5 **Chomiak J**, Junge A, Peterson L, Dvorak J. Severe injuries in football players. Influencing factors. *Am J Sports Med* 2000; **28**: S58-S68 [PMID: 11032109]
- 6 **Giza E**, Fuller C, Junge A, Dvorak J. Mechanisms of foot and ankle injuries in soccer. *Am J Sports Med* 2003; **31**: 550-554 [PMID: 12860543]
- 7 **Badekas T**, Papadakis SA, Vergados N, Galanakis SP, Siapkara A, Forgrave M, Romansky N, Mirones S, Trnka HJ, Delmi M. Foot and ankle injuries during the Athens 2004 Olympic Games. *J Foot Ankle Res* 2009; **2**: 9 [PMID: 19361341 DOI: 10.1186/1757-1146-2-9]
- 8 **Dvorak J**, Junge A, Derman W, Schweltnus M. Injuries and illnesses of football players during the 2010 FIFA World Cup. *Br J Sports Med* 2011; **45**: 626-630 [PMID: 21257668 DOI: 10.1136/bjism.2010.079905]
- 9 **Jain N**, Murray D, Kemp S, Calder J. Frequency and trends in foot and ankle injuries within an English Premier League Football Club using a new impact factor of injury to identify a focus for injury prevention. *Foot Ankle Surg* 2014; **20**: 237-240 [PMID: 25457658 DOI: 10.1016/j.fas.2014.05.004]
- 10 **Karlsson J**. Are sports related injuries expensive? *Scand J Med Sci Sports* 2005; **15**: 1-2 [PMID: 15679565 DOI: 10.1111/j.1600-0838.2005.00444.x]
- 11 **Pritchett JW**. Cost of high school soccer injuries. *Am J Sports Med* 1981; **9**: 64-66 [PMID: 7468903 DOI: 10.1177/03635465810900116]
- 12 **Kofotolis ND**, Kellis E, Vlachopoulos SP. Ankle sprain injuries and risk factors in amateur soccer players during a 2-year period. *Am J Sports Med* 2007; **35**: 458-466 [PMID: 17218660 DOI: 10.1177/0363546506294857]
- 13 **Woods C**, Hawkins R, Hulse M, Hodson A. The Football Association Medical Research Programme: an audit of injuries in professional football: an analysis of ankle sprains. *Br J Sports Med* 2003; **37**: 233-238 [PMID: 12782548 DOI: 10.1136/bjism.37.3.233]
- 14 **Andersen TE**, Floerens TW, Arnason A, Bahr R. Video analysis of the mechanisms for ankle injuries in football. *Am J Sports Med* 2004; **32**: 69S-79S [PMID: 14754862 DOI: 10.1177/0363546503262023]
- 15 **Freeman MA**, Dean MR, Hanham IW. The etiology and prevention of functional instability of the foot. *J Bone Joint Surg Br* 1965; **47**: 678-685 [PMID: 5846767]
- 16 **Hubbard-Turner T**. Relationship between mechanical ankle joint laxity and subjective function. *Foot Ankle Int* 2012; **33**: 852-856 [PMID: 23050709 DOI: 10.3113/FAI.2012.0852]
- 17 **van Dijk CN**, Lim LS, Bossuyt PM, Marti RK. Physical examination is sufficient for the diagnosis of sprained ankles. *J Bone Joint Surg Br* 1996; **78**: 958-962 [PMID: 8951015 DOI: 10.1302/0301-620X78B6.1283]
- 18 **Kerkhoffs GM**, Blankevoort L, van Poll D, Marti RK, van Dijk CN. Anterior lateral ankle ligament damage and anterior talocrural-joint laxity: an overview of the in vitro reports in literature. *Clin Biomech* (Bristol, Avon) 2001; **16**: 635-643 [PMID: 11535344 DOI: 10.1016/S0268-0033(01)00054-7]
- 19 **Agrawal Y**, Carey JP, Hoffman HJ, Sklare DA, Schubert MC. The modified Romberg Balance Test: normative data in U.S. adults. *Otol Neurotol* 2011; **32**: 1309-1311 [PMID: 21892121 DOI: 10.1097/MAO.0b013e31822e5bee]
- 20 **DiGiovanni BF**, Partal G, Baumhauer JF. Acute ankle injury and chronic lateral instability in the athlete. *Clin Sports Med* 2004; **23**: 1-19, v [PMID: 15062581]
- 21 **Loomer R**, Fisher C, Lloyd-Smith R, Sisler J, Cooney T. Osteochondral lesions of the talus. *Am J Sports Med* 1993; **21**: 13-19 [PMID: 8427354 DOI: 10.1177/036354659302100103]
- 22 **Sman AD**, Hiller CE, Refshauge KM. Diagnostic accuracy of clinical tests for diagnosis of ankle syndesmosis injury: a systematic review. *Br J Sports Med* 2013; **47**: 620-628 [PMID: 23222193 DOI: 10.1136/bjsports-2012-091702]
- 23 **Nussbaum ED**, Hosea TM, Sieler SD, Incremona BR, Kessler DE. Prospective evaluation of syndesmosis ankle sprains without diastasis. *Am J Sports Med* 2001; **29**: 31-35 [PMID: 11206253]
- 24 **Oae K**, Takao M, Naito K, Uchio Y, Kono T, Ishida J, Ochi M. Injury of the tibiofibular syndesmosis: value of MR imaging for diagnosis. *Radiology* 2003; **227**: 155-161 [PMID: 12616009 DOI: 10.1148/radiol.2271011865]
- 25 **Sarig-Bahat H**, Krasovsky A, Sprecher E. Evaluation of clinical

- methods for peroneal muscle testing. *Physiother Res Int* 2013; **18**: 55-62 [PMID: 22911954 DOI: 10.1002/pri.1534]
- 26 **Raikin SM.** Intrasheath subluxation of the peroneal tendons. Surgical technique. *J Bone Joint Surg Am* 2009; **91** Suppl 2 Pt 1: 146-155 [PMID: 19255207 DOI: 10.2106/JBJS.H.01356]
- 27 **Staresinic M, Bakota B, Japjec M, Culjak V, Zgaljardic I, Sebecic B.** Isolated inferior peroneal retinaculum tear in professional soccer players. *Injury* 2013; **44** Suppl 3: S67-S70 [PMID: 24060023 DOI: 10.1016/S0020-1383(13)70202-X]
- 28 **Linde F, Hvass I, Jürgensen U, Madsen F.** Early mobilizing treatment in lateral ankle sprains. Course and risk factors for chronic painful or function-limiting ankle. *Scand J Rehabil Med* 1986; **18**: 17-21 [PMID: 3715426]
- 29 **Eiff MP, Smith AT, Smith GE.** Early mobilization versus immobilization in the treatment of lateral ankle sprains. *Am J Sports Med* 1994; **22**: 83-88 [PMID: 8129116 DOI: 10.1177/036354659402200115]
- 30 **Bleakley CM, O'Connor SR, Tully MA, Rocke LG, Macauley DC, Bradbury I, Keegan S, McDonough SM.** Effect of accelerated rehabilitation on function after ankle sprain: randomised controlled trial. *BMJ* 2010; **340**: c1964 [PMID: 20457737 DOI: 10.1136/bmj.c1964]
- 31 **Lamb SE, Marsh JL, Hutton JL, Nakash R, Cooke MW.** Mechanical supports for acute, severe ankle sprain: a pragmatic, multicentre, randomised controlled trial. *Lancet* 2009; **373**: 575-581 [PMID: 19217992 DOI: 10.1016/S0140-6736(09)60206-3]
- 32 **Kerkhoffs GM, Rowe BH, Assendelft WJ, Kelly K, Struijs PA, van Dijk CN.** Immobilisation and functional treatment for acute lateral ankle ligament injuries in adults. *Cochrane Database Syst Rev* 2002; **(3)**: CD003762 [PMID: 12137710]
- 33 **Balduini FC, Vegso JJ, Torg JS, Torg E.** Management and rehabilitation of ligamentous injuries to the ankle. *Sports Med* 1987; **4**: 364-380 [PMID: 3313619 DOI: 10.2165/00007256-198704050-00004]
- 34 **Safran MR, Zachazewski JE, Benedetti RS, Bartolozzi AR, Mandelbaum R.** Lateral ankle sprains: a comprehensive review part 2: treatment and rehabilitation with an emphasis on the athlete. *Med Sci Sports Exerc* 1999; **31**: S438-S447 [PMID: 10416545 DOI: 10.1097/00005768-199907001-00005]
- 35 **McGuine TA, Keene JS.** The effect of a balance training program on the risk of ankle sprains in high school athletes. *Am J Sports Med* 2006; **34**: 1103-1111 [PMID: 16476915 DOI: 10.1177/0363546505284191]
- 36 **Mohammadi F.** Comparison of 3 preventive methods to reduce the recurrence of ankle inversion sprains in male soccer players. *Am J Sports Med* 2007; **35**: 922-926 [PMID: 17379918 DOI: 10.1177/0363546507299259]
- 37 **Karlsson J.** [Ankle braces prevent ligament injuries]. *Lakartidningen* 2002; **99**: 3486-3489 [PMID: 12362747]
- 38 **Sammarco VJ.** Complications of lateral ankle ligament reconstruction. *Clin Orthop Relat Res* 2001; **(391)**: 123-132 [PMID: 11603660]
- 39 **Gross MT, Liu HY.** The role of ankle bracing for prevention of ankle sprain injuries. *J Orthop Sports Phys Ther* 2003; **33**: 572-577 [PMID: 14620786 DOI: 10.2519/jospt.2003.33.10.572]
- 40 **Kennedy JG, Smyth NA, Fansa AM, Murawski CD.** Anatomic lateral ligament reconstruction in the ankle: a hybrid technique in the athletic population. *Am J Sports Med* 2012; **40**: 2309-2317 [PMID: 22879402 DOI: 10.1177/0363546512455397]
- 41 **Liu SH, Baker CL.** Comparison of lateral ankle ligamentous reconstruction procedures. *Am J Sports Med* 1994; **22**: 313-317 [PMID: 8037269 DOI: 10.1177/036354659402200303]
- 42 **Maffulli N, Ferran NA.** Management of acute and chronic ankle instability. *J Am Acad Orthop Surg* 2008; **16**: 608-615 [PMID: 18832604]
- 43 **Guillo S, Bauer T, Lee JW, Takao M, Kong SW, Stone JW, Mangone PG, Molloy A, Perera A, Pearce CJ, Michels F, Toumé Y, Ghorbani A, Calder J.** Consensus in chronic ankle instability: aetiology, assessment, surgical indications and place for arthroscopy. *Orthop Traumatol Surg Res* 2013; **99**: S411-S419 [PMID: 24268842 DOI: 10.1016/j.otsr.2013.10.009]
- 44 **Hua Y, Chen S, Li Y, Chen J, Li H.** Combination of modified Broström procedure with ankle arthroscopy for chronic ankle instability accompanied by intra-articular symptoms. *Arthroscopy* 2010; **26**: 524-528 [PMID: 20362833 DOI: 10.1016/j.arthro.2010.02.002]
- 45 **Choi WJ, Lee JW, Han SH, Kim BS, Lee SK.** Chronic lateral ankle instability: the effect of intra-articular lesions on clinical outcome. *Am J Sports Med* 2008; **36**: 2167-2172 [PMID: 18669983 DOI: 10.1177/0363546508319050]
- 46 **Kerkhoffs GM, Tol JL.** A twist on the athlete's ankle twist: some ankles are more equal than others. *Br J Sports Med* 2012; **46**: 835-836 [PMID: 22966152 DOI: 10.1136/bjsports-2012-091493]
- 47 **Verhagen EA, Van der Beek AJ, Bouter LM, Bahr RM, Van Mechelen W.** A one season prospective cohort study of volleyball injuries. *Br J Sports Med* 2004; **38**: 477-481 [PMID: 15273190 DOI: 10.1136/bjism.2003.005785]
- 48 **van den Bekerom MP, Kerkhoffs GM, McCollum GA, Calder JD, van Dijk CN.** Management of acute lateral ankle ligament injury in the athlete. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1390-1395 [PMID: 23108678 DOI: 10.1007/s00167-012-2252-7]
- 49 **Maffulli N, Del Buono A, Maffulli GD, Oliva F, Testa V, Capasso G, Denaro V.** Isolated anterior talofibular ligament Broström repair for chronic lateral ankle instability: 9-year follow-up. *Am J Sports Med* 2013; **41**: 858-864 [PMID: 23388673 DOI: 10.1177/0363546512474967]
- 50 **Nery C, Raduan F, Del Buono A, Asaumi ID, Cohen M, Maffulli N.** Arthroscopic-assisted Broström-Gould for chronic ankle instability: a long-term follow-up. *Am J Sports Med* 2011; **39**: 2381-2388 [PMID: 21803979 DOI: 10.1177/0363546511416069]
- 51 **Parlomas G, Hannon CP, Murawski CD, Smyth NA, Ma Y, Kerkhoffs GM, van Dijk CN, Karlsson J, Kennedy JG.** Treatment of chronic syndesmosis injury: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1931-1939 [PMID: 23620248 DOI: 10.1007/s00167-013-2515-y]
- 52 **Del Buono A, Florio A, Boccanera MS, Maffulli N.** Syndesmosis injuries of the ankle. *Curr Rev Musculoskelet Med* 2013; **6**: 313-319 [PMID: 23943273 DOI: 10.1007/s12178-013-9183-x]
- 53 **Osahr DC, Drakos MC, O'Loughlin PF, Lyman S, Barnes RP, Kennedy JG, Warren RF.** Syndesmosis and lateral ankle sprains in the National Football League. *Orthopedics* 2013; **36**: e1378-e1384 [PMID: 24200441 DOI: 10.3928/01477447-20131021-18]
- 54 **Thornes B, Shannon F, Guiney AM, Hession P, Masterson E.** Suture-button syndesmosis fixation: accelerated rehabilitation and improved outcomes. *Clin Orthop Relat Res* 2005; **(431)**: 207-212 [PMID: 15685077]
- 55 **Rigby RB, Cottom JM.** Does the Arthrex TightRope® provide maintenance of the distal tibiofibular syndesmosis? A 2-year follow-up of 64 TightRopes® in 37 patients. *J Foot Ankle Surg* 2013; **52**: 563-567 [PMID: 23770192 DOI: 10.1053/j.jfas.2013.04.013]
- 56 **Chuckpaiwong B, Berkson EM, Theodore GH.** Microfracture for osteochondral lesions of the ankle: outcome analysis and outcome predictors of 105 cases. *Arthroscopy* 2008; **24**: 106-112 [PMID: 18182210 DOI: 10.1016/j.arthro.2007.07.022]
- 57 **Saxena A, Eakin C.** Articular talar injuries in athletes: results of microfracture and autogenous bone graft. *Am J Sports Med* 2007; **35**: 1680-1687 [PMID: 17656737 DOI: 10.1177/0363546507303561]
- 58 **O'Loughlin PF, Heyworth BE, Kennedy JG.** Current concepts in the diagnosis and treatment of osteochondral lesions of the ankle. *Am J Sports Med* 2010; **38**: 392-404 [PMID: 19561175 DOI: 10.1177/0363546509336336]
- 59 **Hintermann B, Regazzoni P, Lampert C, Stutz G, Gächter A.** Arthroscopic findings in acute fractures of the ankle. *J Bone Joint Surg Br* 2000; **82**: 345-351 [PMID: 10813167 DOI: 10.1302/0301-620X.82B3.10064]
- 60 **Ferkel RD, Flannigan BD, Elkins BS.** Magnetic resonance imaging of the foot and ankle: correlation of normal anatomy with pathologic conditions. *Foot Ankle* 1991; **11**: 289-305 [PMID: 1674712 DOI: 10.1177/107110079101100506]
- 61 **Potter HG, Chong le R.** Magnetic resonance imaging assessment of chondral lesions and repair. *J Bone Joint Surg Am* 2009; **91**

- Suppl 1: 126-131 [PMID: 19182039 DOI: 10.2106/JBJS.H.01386]
- 62 **Hannon CP**, Smyth NA, Murawski CD, Savage-Elliott I, Deyer TW, Calder JD, Kennedy JG. Osteochondral lesions of the talus: aspects of current management. *Bone Joint J* 2014; **96-B**: 164-171 [PMID: 24493179 DOI: 10.1302/0301-620X.96B2.31637]
- 63 **Choi WJ**, Park KK, Kim BS, Lee JW. Osteochondral lesion of the talus: is there a critical defect size for poor outcome? *Am J Sports Med* 2009; **37**: 1974-1980 [PMID: 19654429 DOI: 10.1177/0363546509335765]
- 64 **Paul J**, Sagstetter M, Lämmle L, Spang J, El-Azab H, Imhoff AB, Hinterwimmer S. Sports activity after osteochondral transplantation of the talus. *Am J Sports Med* 2012; **40**: 870-874 [PMID: 22268232 DOI: 10.1177/0363546511435084]
- 65 **Hangody L**, Dobos J, Baló E, Pánics G, Hangody LR, Berkes I. Clinical experiences with autologous osteochondral mosaicplasty in an athletic population: a 17-year prospective multicenter study. *Am J Sports Med* 2010; **38**: 1125-1133 [PMID: 20360608 DOI: 10.1177/0363546509360405]
- 66 **Niemeyer P**, Salzmann G, Schmal H, Mayr H, Südkamp NP. Autologous chondrocyte implantation for the treatment of chondral and osteochondral defects of the talus: a meta-analysis of available evidence. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 1696-1703 [PMID: 22037894 DOI: 10.1007/s00167-011-1729-0]
- 67 **Fortier LA**, Potter HG, Rickey EJ, Schnabel LV, Foo LF, Chong LR, Stokol T, Cheatham J, Nixon AJ. Concentrated bone marrow aspirate improves full-thickness cartilage repair compared with microfracture in the equine model. *J Bone Joint Surg Am* 2010; **92**: 1927-1937 [PMID: 20720135 DOI: 10.2106/JBJS.I.01284]
- 68 **Smyth NA**, Murawski CD, Fortier LA, Cole BJ, Kennedy JG. Platelet-rich plasma in the pathologic processes of cartilage: review of basic science evidence. *Arthroscopy* 2013; **29**: 1399-1409 [PMID: 23669235 DOI: 10.1016/j.arthro.2013.03.004]
- 69 **Mei-Dan O**, Carmont MR, Laver L, Mann G, Maffulli N, Nyska M. Platelet-rich plasma or hyaluronate in the management of osteochondral lesions of the talus. *Am J Sports Med* 2012; **40**: 534-541 [PMID: 22253252 DOI: 10.1177/0363546511431238]
- 70 **Moustafa El-Sayed AM**. Arthroscopic treatment of anterolateral impingement of the ankle. *J Foot Ankle Surg* 2010; **49**: 219-223 [PMID: 20350820 DOI: 10.1053/j.jfas.2010.02.005]
- 71 **Ferkel RD**, Karzel RP, Del Pizzo W, Friedman MJ, Fischer SP. Arthroscopic treatment of anterolateral impingement of the ankle. *Am J Sports Med* 1991; **19**: 440-446 [PMID: 1962707 DOI: 10.1177/036354659101900504]
- 72 **Guhl JF**. New concepts (distraction) in ankle arthroscopy. *Arthroscopy* 1988; **4**: 160-167 [PMID: 3166653 DOI: 10.1016/S0749-8063(88)80020-3]
- 73 **Cutsurios AM**, Saltrick KR, Wagner J, Catanzariti AR. Arthroscopic arthroplasty of the ankle joint. *Clin Podiatr Med Surg* 1994; **11**: 449-467 [PMID: 7954211]
- 74 **Tol JL**, van Dijk CN. Anterior ankle impingement. *Foot Ankle Clin* 2006; **11**: 297-310, vi [PMID: 16798513]
- 75 **Zwiers R**, Wiegerinck JI, Murawski CD, Smyth NA, Kennedy JG, van Dijk CN. Surgical treatment for posterior ankle impingement. *Arthroscopy* 2013; **29**: 1263-1270 [PMID: 23541613 DOI: 10.1016/j.arthro.2013.01.029]
- 76 **Endele D**, Jung C, Bauer G, Mauch F. Value of MRI in diagnosing injuries after ankle sprains in children. *Foot Ankle Int* 2012; **33**: 1063-1068 [PMID: 23199854 DOI: 10.3113/FAI.2012.1063]
- 77 **Ferkel RD**, Tyorkin M, Applegate GR, Heinen GT. MRI evaluation of anterolateral soft tissue impingement of the ankle. *Foot Ankle Int* 2010; **31**: 655-661 [PMID: 20727312 DOI: 10.3113/FAI.2010.0655]
- 78 **Villarreal JM**, Cerecedo RB, Cal y Mayor FF, González IL. [Arthroscopic treatment for anterolateral ankle impingement of athletes]. *Acta Ortop Mex* 2008; **22**: 103-106 [PMID: 18669311]
- 79 **DeBerardino TM**, Arciero RA, Taylor DC. Arthroscopic treatment of soft-tissue impingement of the ankle in athletes. *Arthroscopy* 1997; **13**: 492-498 [PMID: 9276057 DOI: 10.1016/S0749-8063(97)90129-8]
- 80 **Nihal A**, Rose DJ, Trepman E. Arthroscopic treatment of anterior ankle impingement syndrome in dancers. *Foot Ankle Int* 2005; **26**: 908-912 [PMID: 16309602]
- 81 **McMurray T**. Footballer's ankle. *J Bone Joint Surg BR* 1950; **32**: 68-69
- 82 **Tol JL**, Slim E, van Soest AJ, van Dijk CN. The relationship of the kicking action in soccer and anterior ankle impingement syndrome. A biomechanical analysis. *Am J Sports Med* 2002; **30**: 45-50 [PMID: 11798995]
- 83 **Biedert R**. Anterior ankle pain in sports medicine: aetiology and indications for arthroscopy. *Arch Orthop Trauma Surg* 1991; **110**: 293-297 [PMID: 1747309 DOI: 10.1007/BF00443461]
- 84 **Tol JL**, Verheyen CP, van Dijk CN. Arthroscopic treatment of anterior impingement in the ankle. *J Bone Joint Surg Br* 2001; **83**: 9-13 [PMID: 11245545 DOI: 10.1302/0301-620X.83B1.10571]
- 85 **Tol JL**, van Dijk CN. Etiology of the anterior ankle impingement syndrome: a descriptive anatomical study. *Foot Ankle Int* 2004; **25**: 382-386 [PMID: 15215021]
- 86 **van Dijk CN**, Tol JL, Verheyen CC. A prospective study of prognostic factors concerning the outcome of arthroscopic surgery for anterior ankle impingement. *Am J Sports Med* 1997; **25**: 737-745 [PMID: 9397259 DOI: 10.1177/036354659702500603]
- 87 **van Dijk CN**, Wessel RN, Tol JL, Maas M. Oblique radiograph for the detection of bone spurs in anterior ankle impingement. *Skeletal Radiol* 2002; **31**: 214-221 [PMID: 11904689 DOI: 10.1007/s00256-002-0477-0]
- 88 **Murawski CD**, Kennedy JG. Anteromedial impingement in the ankle joint: outcomes following arthroscopy. *Am J Sports Med* 2010; **38**: 2017-2024 [PMID: 20479141 DOI: 10.1177/0363546510369335]
- 89 **Hamilton WG**, Geppert MJ, Thompson FM. Pain in the posterior aspect of the ankle in dancers. Differential diagnosis and operative treatment. *J Bone Joint Surg Am* 1996; **78**: 1491-1500 [PMID: 8876576]
- 90 **Hedrick MR**, McBryde AM. Posterior ankle impingement. *Foot Ankle Int* 1994; **15**: 2-8 [PMID: 7981792 DOI: 10.1177/107110079401500102]
- 91 **van Dijk CN**, Reilingh ML, Zengerink M, van Bergen CJ. Osteochondral defects in the ankle: why painful? *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 570-580 [PMID: 20151110 DOI: 10.1007/s00167-010-1064-x]
- 92 **Bureau NJ**, Cardinal E, Hobden R, Aubin B. Posterior ankle impingement syndrome: MR imaging findings in seven patients. *Radiology* 2000; **215**: 497-503 [PMID: 10796931 DOI: 10.1148/radiology.215.2.r00ma01497]
- 93 **Dipaola JD**, Nelson DW, Colville MR. Characterizing osteochondral lesions by magnetic resonance imaging. *Arthroscopy* 1991; **7**: 101-104 [PMID: 2009106 DOI: 10.1016/0749-8063(91)90087-E]
- 94 **Robinson P**, Bollen SR. Posterior ankle impingement in professional soccer players: effectiveness of sonographically guided therapy. *AJR Am J Roentgenol* 2006; **187**: W53-W58 [PMID: 16794139 DOI: 10.2214/AJR.05.0614]
- 95 **Calder JD**, Sexton SA, Pearce CJ. Return to training and playing after posterior ankle arthroscopy for posterior impingement in elite professional soccer. *Am J Sports Med* 2010; **38**: 120-124 [PMID: 19966105 DOI: 10.1177/0363546509346390]
- 96 **Smyth NA**, Murawski CD, Levine DS, Kennedy JG. Hindfoot arthroscopic surgery for posterior ankle impingement: a systematic surgical approach and case series. *Am J Sports Med* 2013; **41**: 1869-1876 [PMID: 23720445 DOI: 10.1177/0363546513489489]
- 97 **van Dijk CN**, de Leeuw PA, Scholten PE. Hindfoot endoscopy for posterior ankle impingement. Surgical technique. *J Bone Joint Surg Am* 2009; **91** Suppl 2: 287-298 [PMID: 19805591 DOI: 10.2106/jbjs.i.00445]
- 98 **Smyth NA**, Zwiers R, Wiegerinck JI, Hannon CP, Murawski CD, van Dijk CN, Kennedy JG. Posterior hindfoot arthroscopy: a review. *Am J Sports Med* 2014; **42**: 225-234 [PMID: 23868522 DOI: 10.1177/0363546513491213]
- 99 **Scholten PE**, Sierevelt IN, van Dijk CN. Hindfoot endoscopy for posterior ankle impingement. *J Bone Joint Surg Am* 2008; **90**:

- 2665-2672 [PMID: 19047712 DOI: 10.2106/JBJS.F.00188]
- 100 **Willits K**, Sonneveld H, Amendola A, Giffin JR, Griffin S, Fowler PJ. Outcome of posterior ankle arthroscopy for hindfoot impingement. *Arthroscopy* 2008; **24**: 196-202 [PMID: 18237704 DOI: 10.1016/j.arthro.2007.08.025]
- 101 **Orchard J**. Is there a relationship between ground and climatic conditions and injuries in football? *Sports Med* 2002; **32**: 419-432 [PMID: 12015804 DOI: 10.2165/00007256-200232070-00002]
- 102 **Gehring D**, Rott F, Stapelfeldt B, Gollhofer A. Effect of soccer shoe cleats on knee joint loads. *Int J Sports Med* 2007; **28**: 1030-1034 [PMID: 17455123 DOI: 10.1055/s-2007-965000]
- 103 **Nigg BM**, Segesser B. The influence of playing surfaces on the load on the locomotor system and on football and tennis injuries. *Sports Med* 1988; **5**: 375-385 [PMID: 3135565 DOI: 10.2165/00007256-198805060-00003]
- 104 **Ford KR**, Manson NA, Evans BJ, Myer GD, Gwin RC, Heidt RS, Hewett TE. Comparison of in-shoe foot loading patterns on natural grass and synthetic turf. *J Sci Med Sport* 2006; **9**: 433-440 [PMID: 16672191 DOI: 10.1016/j.jsams.2006.03.019]
- 105 **Queen RM**, Charnock BL, Garrett WE, Hardaker WM, Sims EL, Moorman CT. A comparison of cleat types during two football-specific tasks on FieldTurf. *Br J Sports Med* 2008; **42**: 278-284; discussion 284 [PMID: 17717058 DOI: 10.1136/bjism.2007.036517]
- 106 **Orchard JW**, Chivers I, Aldous D, Bennell K, Seward H. Rye grass is associated with fewer non-contact anterior cruciate ligament injuries than bermuda grass. *Br J Sports Med* 2005; **39**: 704-709 [PMID: 16183765 DOI: 10.1136/bjism.2004.017756]
- 107 **Giza E**, Mithöfer K, Farrell L, Zarins B, Gill T. Injuries in women's professional soccer. *Br J Sports Med* 2005; **39**: 212-216; discussion 212-216 [PMID: 15793089]
- 108 **Prisk VR**, Imhauser CW, O'Loughlin PF, Kennedy JG. Lateral ligament repair and reconstruction restore neither contact mechanics of the ankle joint nor motion patterns of the hindfoot. *J Bone Joint Surg Am* 2010; **92**: 2375-2386 [PMID: 20962188 DOI: 10.2106/JBJS.I.00869]

P- Reviewer: Fernandez-Fairen M, Macheras GA
S- Editor: Tian YL **L- Editor:** A **E- Editor:** Li D



Mechanical and cellular processes driving cervical myelopathy

Roisin T Dolan, Joseph S Butler, John M O'Byrne, Ashley R Poynton

Roisin T Dolan, Department of Trauma and Orthopaedic Surgery, Waterford Regional Hospital, X91 ER8E Waterford, Ireland

Joseph S Butler, National Spinal Injuries Unit, Department of Trauma and Orthopaedic Surgery, Mater Misericordiae University Hospital, D07 AX57 Dublin, Ireland

John M O'Byrne, Department of Trauma and Orthopaedic Surgery, Royal College of Surgeons in Ireland, Cappagh National Orthopaedic Hospital, D11 K316 Dublin, Ireland

Ashley R Poynton, Department of Trauma and Orthopaedic Surgery, Mater Private Hospital, D07 WKW8 Dublin, Ireland

Author contributions: All authors had significant contributions to the conception and design of the review article; Dolan RT and Butler JS contributed to drafting the article; O'Byrne JM and Poynton AR were responsible for revising it critically for important intellectual content.

Conflict-of-interest statement: The authors declare no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dr. Roisin T Dolan, MA, MD, MRCSI, Department of Trauma and Orthopaedic Surgery, Waterford Regional Hospital, Dunmore Rd., X91 ER8E Waterford, Ireland. roshdolan@hotmail.com
Telephone: +353-51-858000
Fax: +353-51-858001

Received: December 26, 2014
Peer-review started: December 29, 2014
First decision: February 10, 2015
Revised: October 12, 2015
Accepted: November 3, 2015

Article in press: November 4, 2015
Published online: January 18, 2016

Abstract

Cervical myelopathy is a well-described clinical syndrome that may evolve from a combination of etiological mechanisms. It is traditionally classified by cervical spinal cord and/or nerve root compression which varies in severity and number of levels involved. The vast array of clinical manifestations of cervical myelopathy cannot fully be explained by the simple concept that a narrowed spinal canal causes compression of the cord, local tissue ischemia, injury and neurological impairment. Despite advances in surgical technology and treatment innovations, there are limited neuro-protective treatments for cervical myelopathy, which reflects an incomplete understanding of the pathophysiological processes involved in this disease. The aim of this review is to provide a comprehensive overview of the key pathophysiological processes at play in the development of cervical myelopathy.

Key words: Cervical myelopathy; Cervical spine; Neck pain

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The pathophysiology of cervical myelopathy involves a combination of mechanical static and dynamic factors, triggering a cascade of biomolecular changes to include ischemia, excitotoxicity, neuroinflammation and apoptosis. Development of targeted neuro-protective treatment strategies, specifically modulating these molecular pathways, may optimize neurological recovery following surgical decompression. The aim of this review is to provide an overview of the pathophysiological processes at play in the development of cervical myelopathy.

Dolan RT, Butler JS, O'Byrne JM, Poynton AR. Mechanical and cellular processes driving cervical myelopathy. *World J Orthop* 2016; 7(1): 20-29 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/20.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.20>

INTRODUCTION

Cervical myelopathy is the most commonly reported spinal cord pathology globally in the > 55 years age cohort^[1-3]. Twenty-five percent of spinal cord dysfunction in the United Kingdom is caused by cervical spondylotic myelopathy^[4]. The exact biostatistics in relation to the disease remains unknown, however there exists a male preponderance at a ratio of 2.7:1^[5]. Originally detailed by Stookey^[6] in 1928, compression of the cord by cartilaginous degenerative disc nodules was the primary pathogenic mechanism attributed to this disorder. The key neuropathological characteristics of cervical myelopathy include cystic cavitation, gliosis, Wallerian degeneration of descending and ascending tracts, and loss of anterior horn cells^[7,8].

Clinically, cervical myelopathy presents as progressive spinal cord impairment. Symptoms include distorted proprioception, weakness and paresthesia of the hands, spasticity of the lower limbs with resultant gait disturbance, and pyramidal and posterior cord dysfunction^[9]. In addition to motor and sensory sequelae, neuropathic pain and functional limitations can be devastating, resulting in significant physical and socioeconomically restrictions for previously healthy individuals. Thus, there exists an urgent requirement to clearly define the pathobiology of the cervical myelopathy to assist discovery of translational interventional strategies.

Researchers have previously postulated that a narrowed spondylotic spinal canal causes compression of the enclosed cord potentially causing local neural ischemia and neurological impairment. The aetiology of cervical cord compression is multifactorial with contributions from disc herniation alone; and osteophytic spur overgrowth in the spinal canal referred to as spondylosis. A decrease in vertebral canal diameter as a consequence of age-related degenerative changes of the joints, intervertebral discs, and ligaments of the cervical vertebrae, significantly contributing to cord compression^[1]. Infolding of the ligamentum flavum and facet joint capsule can distort spinal canal anatomy and foraminal dimensions^[10]. However, this simple anatomic model has been challenged by falling short of explaining the array of clinical presentations in cervical myelopathy, specifically development of neurological impairment in the absence of static spinal cord compression^[11]. Whilst the aetiology of cervical myelopathy is thought to be multifactorial including contributions from age-related degeneration, mechanical stress and biochemical factors, a genetic predisposition has been revisited, due to recent

evidence of familial clustering in population studies^[12].

Despite advances in the surgical management of cervical myelopathy in addition to earlier diagnosis facilitated by advances in diffusion tensor magnetic resonance imaging (MRI) and kinetic MRI, a significant proportion of patients suffer residual neurological sequelae as a consequence of irreversible cord injury^[13-17]. Thus, implementation of neuro-protective interventions as an adjunct to surgical decompression may optimise patient outcomes for cervical myelopathy.

THE ANATOMIC BASIS OF CERVICAL SPONDYLOTIC MYELOPATHY

In the context of progressive age-related degenerative changes, clinically significant cervical spondylotic myelopathy typically presents in late adulthood. These changes include cervical disc degeneration, osteophytic spur formation and transverse bar formation and osteoarthritic facet hypertrophy. Age-related degenerative changes with respect to supporting ligaments include posterior longitudinal ligament calcification and ligamentum flavum thickening^[18-22]. The concept of dynamic stenosis represents progressive impingement on the spinal canal, resulting in transient spinal cord compression during physiological cervical range of motion. However, in some cases, dynamic stenosis may evolve into static compression of the spinal cord, manifesting clinically as classic cervical spondylotic myelopathy.

MECHANISMS OF CERVICAL MYELOPATHY

Although the specific pathophysiological mechanisms contributing to cervical myelopathy remain ambiguous, it is considered a manifestation of long-tract signs resulting from multifactorial compression on the cervical spinal cord^[10]. Key factors in the development of cervical myelopathy are categorized as either static or dynamic mechanical factors, resulting in direct injury to neurons and glia, which in turn triggers a cascade of secondary cellular mechanisms (Table 1)^[1,23].

Static mechanical factors

Spondylosis and disc degeneration: Progressive cervical spondylotic changes are a key feature in the pathogenesis of cervical myelopathy due to an increase in the compressive extrinsic canal forces (Figure 1). With advancing age, the intervertebral discs cannot bear load due to a combination of factors to include medial splitting of the disc and gradual loss of the nucleus pulposus. It is this disc degeneration that stimulates a cascade of progressive changes resulting in cervical canal stenosis and the development of cervical spondylotic myelopathy^[24]. Anterolateral uncovertebral process flattening increases the load imposed on vertebral articular cartilage. This promotes the

Table 1 Pathophysiological factors involved in cervical myelopathy

Static factors
Spondylosis
Disc degeneration
Ossification of the posterior longitudinal ligament
Ossification of ligamentum flavum
Congenital stenosis
Other acquired congenital pathology, <i>e.g.</i> , tumors, calcification
Dynamic factors
Changes in neck flexion/extension - narrow spinal canal
Biomolecular factors
Ischemic injury - compression of spinal cord vasculature
Glutamate - mediated excitotoxicity
Oligodendrocyte and neuronal apoptosis

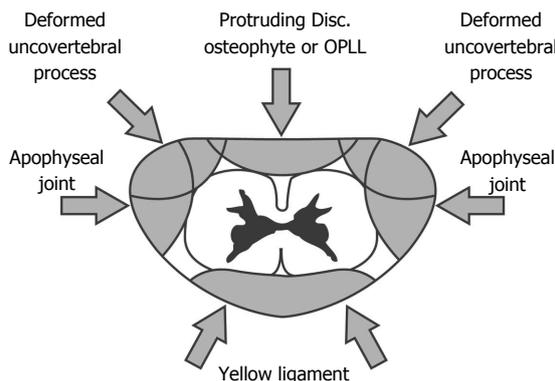


Figure 1 Degenerative changes that contribute to extrinsic compression of the spinal cord in cervical myelopathy. OPLL: Ossification of the posterior longitudinal ligament.

development of osteophytic spurs. A combination of osteophytic spur overgrowth ventrally and buckling of the ligamentum flavum posteriorly, can lead to a circumferential mechanical compression of the spinal cord inducing cervical myelopathy^[25]. Additionally, the conformational change in bony structures can compromise the integrity of the vertebral artery and spinal nerve leading to demyelination of ascending and descending tracts and chronic pain^[1]. Radiological assessment is key, as it assists differentiation of disk-related neck pain, radiculopathy, and myelopathy. Imaging, in the context of pre-operative planning, also aids localization of the site-specific disease^[26]. Compared with other radiological studies MRI provides an overview of both bony and soft tissue architecture including intervertebral discs, supporting ligaments, and neural structures. Dynamic weight bearing (kinetic) MRI has been hailed as the gold standard modality for cervical spondylotic myelopathy^[15,27]. Myelopathy is represented radiographically with increased cord signal on T2-weighted MRI and a decreased signal on T1-weighted imaging^[28]. Diffusion tensor imaging (DTI) improves pathologic specificity by measuring directional diffusivities, which quantify water diffusion parallel and perpendicular to the white matter tracts^[16,29]. A recent study of the role of DTI in cervical spondylotic myelopathy suggested that DTI may elucidate pathology of the spinal cord before the development of T2 hyperintensity imaging and thus may be a superior imaging modality in the future^[13].

Ectopic ossification of spinal ligaments: Ectopic ossification and calcification of spinal ligaments has also been attributed to the development of spinal canal stenosis and the onset and aggravation of myelopathic symptoms^[1,30]. Ossification of the posterior longitudinal ligament (OPLL) is a common pathology^[20,31]. Pathological compression by OPLL commonly presents with severe myelopathy and can lead to quadraparesis^[32]. The natural course of OPLL suggests a degenerative process as a consequence of environmental factors such as accumulative extrinsic loading on the spine and genetic predisposition. *In vivo*

studies involving the Yoshimura mouse, which develops ossification of the posterior ligaments akin to human OPLL, has identified a mutation within the nucleotide pyrophosphatase (*NPPS*) gene^[31]. Defective *NPPS* results in reduced production of pyrophosphatase, permitting ectopic ossification of spinal ligaments. Recent genetic studies involving the human *NPPS* locus have identified female sex, age (< 35 years) and severe ossification (> 10 ossified vertebra) correlated with susceptibility to and severity of OPLL^[33]. Further studies involving the Zucker fatty rat have propose a role of a missense mutation in the leptin receptor gene in the promotion of ectopic ossification^[34]. Thus, it is credible that *NPPS* and leptin receptor genes function in synergy in the pathogenesis of ectopic ossification and myelopathy. In light of these novel findings, there is a requirement to investigate this association in human OPLL.

It has been postulated that stenosis and subsequent cord compression may occur as a consequence of ossification of ligamentum flavum (OLF)^[21]. The major diagnostic difference is grossly anatomical. In OLF, calcifications allow ligamentum flavum to fuse with adjacent lamina, whereas in OPLL the ligament adheres to the posterior aspects of the vertebral bodies and intervertebral discs. Despite this anatomical disparity, studies report the role of bone morphogenic protein-2 and transforming growth factor- β in matrix hyperplasia and ossification in both OPLL and OLF^[35].

Congenital spinal canal stenosis: It is reported that cervical stenosis has an incidence of approximately 4.9% of the adult population^[36]. Cervical stenosis is influenced by two factors: (1) degenerative cervical spondylosis; and (2) a developmentally narrow canal. Recent cadaveric studies have revealed that females patients and individuals over 60 years old, have narrower canals^[37]. The presence of congenital or developmental canal stenosis is highly predictive of later myelopathic cord dysfunction^[1]. The normal anteroposterior dimensions of the subaxial canal has been reported as 17-18 mm between C3 and C7^[38,39]. Numerous MRI studies have concluded that a congenital sagittal spinal

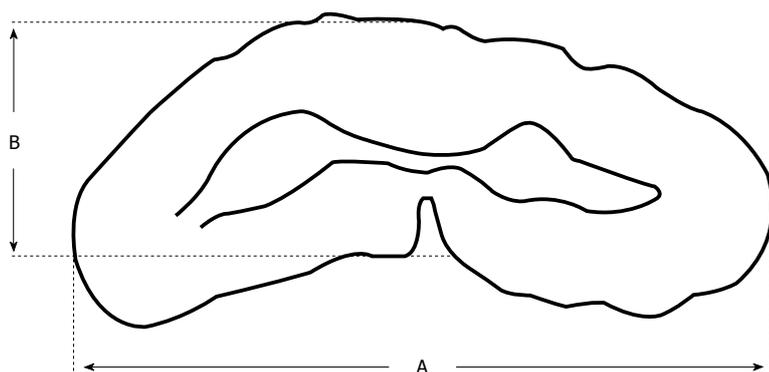


Figure 2 Determination of the anteroposterior compression ratio in patients with cervical myelopathy. $AP = b/a \times 100$. Reprinted with permission. AP: Anteroposterior compression ratio.

canal diameter of < 13 mm is predictive of development of cervical spondylotic myelopathy (CSM)^[18,40]. The shape and cross-sectional area of the cord are important independent predictors of the development of CSM and specifically, of neurologic deficit. A transverse area of cord < 60 mm² and a banana-shaped cord have both been correlated with the clinical presentation of myelopathy^[41,42]. The anteroposterior compression ratio (AP) is calculated by dividing the anterior-posterior diameter of the cord by the transverse diameter of the cord (Figure 2)^[43]. It has been suggested that an AP ratio $< 40\%$ is representative of substantial flattening of the cord and strongly predictive of significant neurologic dysfunction^[43]. MRI has been reported as the most accurate method to quantify spinal canal diameter as it assesses both the bony and soft tissue components when estimating spinal canal diameter. This is particularly relevant in the context of CSM whereby central stenosis is often multifactorial to include both bony and soft tissue pathology, *e.g.*, osteophytic spurring, OPLL and posterior disc protrusion^[44,45]. Spinal MRI for assessment of CSM should include imaging sets obtained in the axial and sagittal planes using a combinations of T1-weighted, and T2-weighted sequences. Fast spin-echo MRI is the best modality to diagnose disc fragments and osteophytes^[46].

Dynamic mechanical factors

Dynamic canal space narrowing: It is intuitive that the extent of dynamic mechanical compression of the spinal cord could be significantly manipulated by movement of the cervical spine. During extremes of flexion and extension, a dynamic canal space of < 11 mm has been reported as a critical level for spinal functioning and is strongly predictive of cervical myelopathy^[38,47]. Hyperextension of the neck causes canal narrowing by inducing buckling the ligamentum flavum and shingling the laminae. This “pincer effect” induces spinal cord compression between the inferior surface of one vertebra and the lamina or ligamentum flavum of the adjacent vertebra^[23,47]. In flexion, the spinal cord lengthens and takes a more anterior position in the canal. If the cord impinges against a disc or vertebral body anteriorly, this will induce a higher intrinsic pressure, resulting in increased axial tension and

potential ischemic injury^[19].

Effects of stretch and shear: Studies suggest that stretch-associated injury is a major contributor to myelopathy. This claim is supported by evidence in numerous experimental models to include neural injury, tethered cord syndrome, and diffuse axonal injury^[11,48,49]. During flexion/extension movements of the spine, elongation of the canal results in longitudinal strain of the spinal cord^[50]. This is consistent with Euler’s Theorem, which implicates distraction of the complex portion of a structure that is placed in a flexion mode. The cord can stretch up to a quarter of its length which can correspond to an elongation of 17.6 mm measured at the level of the cervical spine during neck flexion. The increased stretch at this level results in a significant cord compression, translating to increased stress in the white matter and higher stress in gray matter^[51]. This is further compounded by craniocervical flexion, which results in longitudinal transmission of stretching force and increases in intramedullary pressure in the lower cervical spine^[48]. The rapid occurrence of low-grade mechanical stretching on neural tissues can exceed the biomechanics of the tissue. This can lead disruption of the tissue and may result in transient or permanent neurological injury. Dynamic forces induced by flexion and extension of the spinal column contribute to axial cord strain with potentially detrimental stretch-induced axonal injury^[11]. Cadaveric studies have demonstrated that ongoing longitudinal strain, even within physiological limits, will eventually surpass its material tolerance thereby permitting neurological injury^[19]. In canine models, the elastic modulus of the spinal cord tissue decreases with increasing load. The canine spinal cord stripped of pia begins to rupture at a strain close to that developed in the cervicothoracic spinal cord of humans. Deleterious stresses to the spinal cord should be viewed in aggregate and in the context of movement. In the absence of repetitive movement, viscoelastic relaxation of the spinal cord mitigates stress resulting from deformation^[52]. In a dynamic formulation, cord deformation form an osteophytic spur or calcified disc herniation adds abnormal plane loading and shear to strain resulting from

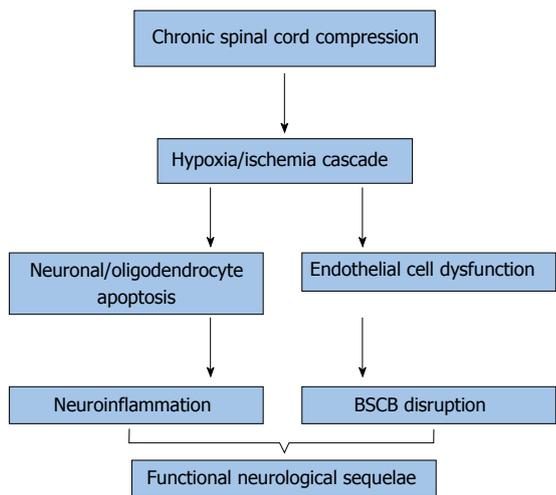


Figure 3 Cellular mechanisms involved in cervical myelopathy. The hypoxia/ischemia cascade results from chronic progressive compression of the cervical spinal cord. This induces extracellular (TNF- α) and intracellular proapoptotic pathways (p-53, JNK), induces neuroinflammation and ultimately, neuronal and oligodendrocyte destruction. Additionally, compromise of the BSCB results from ischemia-induced endothelial cell loss. Increased BSCB permeability alters the cellularity of the spinal cord microenvironment and is thought to further potentiate neuroinflammation. These mechanisms contribute to the upper limb dysfunction, spasticity, and gait disturbances observed in human cervical spondylotic myelopathy. BSCB: Blood-spinal cord barrier; TNF- α : Tumor necrosis factor- α .

flexion at the craniocervical and cervicothoracic junctions, significantly increasing overload stress.

The neurobiology of stretch-associated axonal and myelin injury is now understood as a result of work in primates and other animals and from studies of diffuse axonal injury in the human brain. Numerous studies have reproducibly demonstrated that axonal injury frequently occurs at sites of maximal mechanical stress and occurs as a series of recognized events: Myelin stretch injury, altered axolemmal permeability, calcium entry, cytoskeletal collapse, compaction of neurofilaments and microtubules, disruption of anterograde axonal transport, accumulation of organelles, axon retraction, bulb formation, and secondary axotomy^[11,53,54].

There is clearly support for the contention that myelopathy increases in the presence of abnormal or excessive motion in the neck^[55-57]. It should also be noted that stress is multifactorial and may include elements of gliosis within the spinal cord, acute and chronic changes in cord compliance, and altered gray and white viscoelastic relaxation gradients^[51]. Understanding the deleterious effects of abnormal/excessive neck motion highlights the need to eliminate deformation of the spinal cord by minimizing abnormal mobility, and restoring normal sagittal spinal cord contour.

Cellular mechanisms involved in cervical myelopathy

Sufficient pathophysiologic parallels between traumatic spinal cord injury (SCI) and cervical myelopathy have been identified to warrant a brief discussion of these novel mechanisms^[58]. It has been proposed that primary mechanical injuries caused by static and dynamic forces

to include compression, shear and distraction, induce a secondary injury at the molecular level. Several cellular mechanisms pertaining to these secondary injuries are discussed briefly to include ischemia, glutamatergic toxicity, neuroinflammation and apoptosis (Figure 3)^[59-65].

Ischemic injury: Recent studies propose that progressive ischemia of the spinal cord may be central to the origin of cervical myelopathy^[36]. The association of ischemia and myelopathy was first hypothesised from the observation of hyalinization and hypertrophy of the walls of the anterior spinal artery upon post-mortem histologic evaluation^[66]. Later post-mortem studies of symptomatic cervical myelopathy patients demonstrated further abnormal histologic findings, to include spinal cord ischemic necrosis. Further evidence to implicate spinal cord ischemia in the pathogenesis of cervical myelopathy is that the lower cervical spinal cord, the commonest site of cervical myelopathy, also has the most vulnerable blood supply^[67].

Ischemia of the cord secondary to compression was later proposed following experimental observations in canine models. These studies exposed the vulnerability of corticospinal tracts in ischemia conditions and the development of intramedullary cavitation secondary to peripial arterial plexus ischemia^[66,68-70]. The use of balloon catheters to assess spinal compression in monkeys revealed hypoperfusion through the transverse arterioles originating from the anterior sulcal arteries and intramedullary branches in the central gray matter, upon anterior and posterior compression^[71]. At the cellular level, there is evidence to suggest that oligodendroglia may be hypersensitive to ischemic injury and can apoptose after acute trauma^[61,72,73]. These mechanisms may contribute to the demyelinating process observed in chronic cervical myelopathy^[74]. The role of ischemic injury has also been proposed with evidence of edema and gliosis represented on MRI. T2-weighted MRI can detect high-intensity signal change, and demyelination and necrosis detected as a hypoenhancement on T1-weighted MRI^[75]. MRI changes are an important prognostic indicator. The high intensity signal change seen on T2 images are associated with pathologies that are potentially reversible whereas the low intensity changes seen on T1 images are not. However, it has been proposed that all signal change on MRI is indicative of significant underlying pathology as it is representative of extensive neuronal hypoplasia, glial cell substitution of stroma, and white matter degradation^[76].

Disruption of the blood-spinal cord barrier: It has been postulated that the ongoing cord compression observed in cervical myelopathy results in remodelling of the spinal cord^[36]. This conformational change may result in endothelial cell loss and dysfunction of the local vasculature^[7]. Damage to endothelial cells from resultant ischemia may also impact the integrity of the blood-spinal cord barrier (BSCB). BSCB dysfunction is accompanied by a disruption in vascular permeability leading to cord

edema. BSCB permeability in neurotrauma is viewed as a detrimental event to the central nervous system (CNS), secondary to entry of blood-borne inflammatory mediators and increased edema. However, CSM animal models examining mechanisms of BSCB dysfunction and neuroinflammatory responses, remain incomplete.

Glutamatergic toxicity: Glutamate is the major excitatory neurotransmitter in the human CNS. Excitotoxicity is the capacity of excitatory neurotransmitters to control apoptosis of neuronal and oligodendrocyte cells. In the clinical setting these cellular changes have been observed in multiple neuropathologies to include cerebrovascular accidents, traumatic spinal cord injuries and seizure activity^[77]. Secondary excitotoxicity refers to neuronal and oligodendrocytic dysfunction mediated by glutamate. It is activated by fluctuations in neuronal metabolism, and has been associated with an array of chronic neurodegenerative diseases^[77,78]. Researchers have proposed two structural properties specific to motor neurones that may increase their susceptibility to neurodegeneration. Calcium-mediated toxic events increase their susceptibility to neurodegeneration due to underexpression of both calcium binding proteins and GluR2 AMPA receptors. Based on these findings, future innovations may focus on targeting glutamate receptors in chronic neurodegenerative diseases.

Apoptosis: Apoptosis is defined as programmed cell death, recognised following ischemic and traumatic injury to the CNS^[72,79-81]. Decreased perfusion and subsequent ischemia may be important pro-apoptotic events in cervical myelopathy, given the hypersensitivity of neurons and oligodendrocytes to ischaemic injury. In traumatic SCI, there is thought to be a cascade of degenerative changes at the lesion epicentre and demyelination of tracts distant to the injury^[61]. The delayed degeneration of anterior horn cells in cervical myelopathy may reflect the effects of apoptosis. It is postulated that axonal degeneration is preceded by oligodendrocyte apoptosis in cervical myelopathy. This series of cellular events has been observed in histological analysis of *in vivo* models of spinal cord compression, whereby intact demyelinated axons have been observed in the presence of apoptotic oligodendrocytes^[58,82]. This is of major therapeutic significance given recent evidence supporting the anti-apoptotic role of novel pharmacologic inhibitors of the calcium-activated calpain, c-Jun N-terminal kinase and Fas-mediated apoptotic pathways^[2,83,84]. Targeting these pro-apoptotic receptors in patients with cervical myelopathy may be employed as neuro-protective treatment strategies in attempt to diminish the degree of neural degeneration.

Neuroinflammation: Although neuroinflammation is considered integral to wound healing in the setting of neurotrauma, recent evidence suggests that the inflammatory response is a key player in the pro-apoptotic pathway following this event^[85]. It is becoming apparent

that the innate and adaptive immune responses to acute spinal injuries and chronic cervical myelopathy are dissimilar. Unique to cervical spondylotic myelopathy is a slow inflammatory process, driven by chronic progressive inflammation^[86]. Recruitment of neutrophils, monocytes/macrophages, and lymphocytes has been demonstrated in a human model of CSM^[2]. However, the identity of the beneficial and detrimental inflammatory mediators in this process remains unknown. Future modulation of this inflammatory cascade has the potential to provide a basis for development of therapeutics for chronic spinal compression disorders.

Effect of neuromodulators on CNS microvasculature: Studies regarding the neurovascular complications of cocaine (benzoylmethylecgonine) report that its use exacerbates and accelerates the natural history of neurological pathology. Cocaine is a serotonin-norepinephrine-dopamine reuptake inhibitor that acts as a powerful CNS stimulant. The compound produces vasoconstriction of the CNS microvasculature, including the anterior spinal artery. Additionally, cocaine primes the responsiveness of platelets to arachidonic acid, leading to an increase in thromboxane release and platelet aggregation. Both these mechanisms independently contribute to infarction of the CNS microvasculature, including the spinal cord.

Recent studies have demonstrated a positive correlation between cocaine abuse and CNS infarction of the middle cerebral artery, vertebrobasilar artery territories, anterior spinal artery, and lateral medulla. However, there is a paucity of data relating to the chronic sequelae of cocaine use on the neurological microenvironment. Studies have demonstrated moderate and persistent alterations in cerebral and spinal blood flow and increased incidence of cerebral vasculitis among cocaine users. A recent study sought to establish the effect of chronic cocaine use on post-operative neurological recovery following surgical decompression of the cervical spine in a cohort of 95 patients diagnosed with symptomatic cervical spondylotic myelopathy^[87]. The ability of the spinal cord to heal after surgical decompression is based on the intrinsic ability of the spinal cord to heal itself. Thus, the pre-operative health of the cord is paramount to post-operative improvement. This study revealed that chronic cocaine users had poorer post-operative neurological recovery than non-users and adds further credence to the negative impact of cocaine on spinal cord integrity. These data may influence pre-operative counseling and patient selection in attempt to optimize outcomes following surgical decompression for cervical myelopathy.

Smoking has been identified as a common risk factor for spinal degenerative diseases^[88]. A recent *in vitro* study investigating the effects of nicotine exposure on nucleus pulposus proliferation and extracellular matrix synthesis demonstrated a significant anti-proliferative effect^[89]. This suggests that nicotine may contribute to the pathogenesis of vertebral disc degeneration and the

development of cervical myelopathy however, further *in vivo* studies are required to elucidate its role at the molecular level.

Genetic predisposition to cervical myelopathy

The role of heredity in the development of cervical myelopathy was first suggested by Bull *et al.*^[90] in 1969. Upon evaluation of several hundred cervical spine radiographs, the authors observed a higher prevalence of simultaneous CSM among twins. MRI of the spines of 172 monozygotic and 154 dizygotic twins revealed that heritability accounted for almost three-quarters of all findings, among a cohort of patients with severe CSM^[91].

Flourishing interest in the role of heredity has been supported by evidence of families with a high incidence of CSM^[92,93]. The authors' imply that these cases may represent extreme cases of genetic influence or it may depict the presence of a separate entity classified as "familial cervical spondylosis".

Previous studies have suggested a correlation between variants of collagen gene expression and degenerative intervertebral disc disorders^[94,95]. Collagen IX, a structural component of nucleus pulposus and annulus fibrosis of the intervertebral disc, acts as a bridge between proteins in these tissues. Collagen IX is essential to the proper formation of the collagen II/IX/XI heteropolymer^[96]. Recent studies have suggested that collagen tryptophan IX genetic material influence lumbar disc degeneration in patients with herniated nucleus pulposus. Interestingly, it has recently been demonstrated that patients with collagen IX polymorphisms who are smokers have a significantly higher predisposition to developing cervical myelopathy^[88]. This landmark study suggests that smoking abstinence is important for reducing cervical myelopathy risk in patients with a genetic predisposition.

Despite the paucity of conclusive evidence to clearly delineate the aetiology of CSM, a multifactorial aetiology to include age-related degeneration, biomechanical factors and heredity is supported.

FUTURE INNOVATIONS

Whilst acute SCI models have unveiled some cellular mechanisms involved in the pathobiology of CSM, this unique condition and its specific pathomechanisms are poorly defined. A limitation in advancing our knowledge of CSM has been a paucity of reproducible *in vivo* models to replicate CSM. Several models of acute cord compression have been developed, but relatively little work has focused on the development of an *in vivo* chronic, graded, cervical cord compression^[64,92,97].

However, a recently developed animal model of CSM, employed a chronic compression device on the cervical spine of Sprague-Dawley rats, to achieve chronic and progressive cord compression^[4]. This model has the potential to reproduce quantifiable neurobehavioral, neurophysiological, and neuropathological deficits akin

to human CSM. Ultimately, this innovation may act as an important catalyst in the translation of targeted therapeutic strategies for cervical myelopathy^[4].

Regarding technological advancements, innovations in neuro-imaging will continue to play a key role by facilitating timely diagnosis of soft tissue and osseous pathology in CSM, assist in optimal patient selection for surgical intervention and provide prognostic information in the post-operative period. In addition to advances in kinetic magnetic resonance imaging and DTI, metabolic neuroimaging, has been compared with functional assessments following clinical examination and findings on MRI, of patients selected for surgery for CSM. FDG-PET findings were highly sensitive displayed strong correlations with pre- and postoperative scores, and postoperative rehabilitation^[98,99]. The major limitation of this technology is the poor resolution of PET scans. Despite this, future innovations in PET imaging may allow identification of early spinal cord damage and provide indications for surgical intervention.

CONCLUSION

The cervical spine adapts to the challenges of gravity and the effects of mechanical loading through both structural and biochemical changes. These adaptations may result in significant physical disability, and in turn stimulate altered biochemical pathways. The pathophysiology of CSM involves a combination of static and dynamic mechanical factors, which induce cellular changes to include neuroischemia, excitotoxicity, neuroinflammation and apoptotic events. There exists an urgent requirement for the development of novel neuro-protective treatment strategies to inhibit neural degeneration and optimize neurological recovery following surgical decompression for CSM.

REFERENCES

- 1 **Baptiste DC**, Fehlings MG. Pathophysiology of cervical myelopathy. *Spine J* 2006; **6**: 190S-197S [PMID: 17097538 DOI: 10.1016/j.spinee.2006.04.024]
- 2 **Yu WR**, Liu T, Kiehl TR, Fehlings MG. Human neuropathological and animal model evidence supporting a role for Fas-mediated apoptosis and inflammation in cervical spondylotic myelopathy. *Brain* 2011; **134**: 1277-1292 [PMID: 21490053 DOI: 10.1093/brain/awr054]
- 3 **Toledano M**, Bartleson JD. Cervical spondylotic myelopathy. *Neurol Clin* 2013; **31**: 287-305 [PMID: 23186905 DOI: 10.1016/j.ncl.2012.09.003]
- 4 **Lee J**, Satkunendrarajah K, Fehlings MG. Development and characterization of a novel rat model of cervical spondylotic myelopathy: the impact of chronic cord compression on clinical, neuroanatomical, and neurophysiological outcomes. *J Neurotrauma* 2012; **29**: 1012-1027 [PMID: 21561323 DOI: 10.1089/neu.2010.1709]
- 5 **Broomfield SJ**, Da Cruz M, Gibson WP. Cochlear implants and magnetic resonance scans: A case report and review. *Cochlear Implants Int* 2013; **14**: 51-55 [PMID: 22449316 DOI: 10.1179/17547]
- 6 **Stookey B**. Differential section of the trigeminal root in the surgical treatment of trigeminal neuralgia. *Ann Surg* 1928; **87**: 172-178 [PMID: 17865827]

- 7 **Bohlman HH**, Emery SE. The pathophysiology of cervical spondylosis and myelopathy. *Spine* (Phila Pa 1976) 1988; **13**: 843-846 [PMID: 3057649]
- 8 **Swagerty DL**. Cervical spondylotic myelopathy: a cause of gait disturbance and falls in the elderly. *Kans Med* 1994; **95**: 226-227, 229 [PMID: 7815775]
- 9 **Nakamura I**, Ikegawa S, Okawa A, Okuda S, Koshizuka Y, Kawaguchi H, Nakamura K, Koyama T, Goto S, Toguchida J, Matsushita M, Ochi T, Takaoka K, Nakamura Y. Association of the human NPPS gene with ossification of the posterior longitudinal ligament of the spine (OPLL). *Hum Genet* 1999; **104**: 492-497 [PMID: 10453738 DOI: 10.1007/S004390050993]
- 10 **Rao R**. Neck pain, cervical radiculopathy, and cervical myelopathy: pathophysiology, natural history, and clinical evaluation. *J Bone Joint Surg Am* 2002; **84-A**: 1872-1881 [PMID: 12377921 DOI: 10.1097/00002517-199407020-0000]
- 11 **Henderson FC**, Geddes JF, Vaccaro AR, Woodard E, Berry KJ, Benzel EC. Stretch-associated injury in cervical spondylotic myelopathy: new concept and review. *Neurosurgery* 2005; **56**: 1101-1103; discussion 1101-1103 [PMID: 15854260]
- 12 **Patel AA**, Spiker WR, Daubs M, Brodke DS, Cannon-Albright LA. Evidence of an inherited predisposition for cervical spondylotic myelopathy. *Spine* (Phila Pa 1976) 2012; **37**: 26-29 [PMID: 21252820 DOI: 10.1097/brs.0b013e3182102ede]
- 13 **Kara B**, Celik A, Karadereler S, Ulusoy L, Ganiyusufoglu K, Onat L, Mutlu A, Ornek I, Sirvanci M, Hamzaoglu A. The role of DTI in early detection of cervical spondylotic myelopathy: a preliminary study with 3-T MRI. *Neuroradiology* 2011; **53**: 609-616 [PMID: 21344215 DOI: 10.1007/S00234-011-0844-4]
- 14 **Lao LF**, Zhong GB, Li QY, Liu ZD. Kinetic magnetic resonance imaging analysis of spinal degeneration: a systematic review. *Orthop Surg* 2014; **6**: 294-299 [PMID: 25430713 DOI: 10.1111/OS.12137]
- 15 **Harada T**, Tsuji Y, Mikami Y, Hatta Y, Sakamoto A, Ikeda T, Tamai K, Hase H, Kubo T. The clinical usefulness of preoperative dynamic MRI to select decompression levels for cervical spondylotic myelopathy. *Magn Reson Imaging* 2010; **28**: 820-825 [PMID: 20418043 DOI: 10.1016/j.mri.2010.03.038]
- 16 **Xu J**, Shimony JS, Klawiter EC, Snyder AZ, Trinkaus K, Naismith RT, Benzinger TL, Cross AH, Song SK. Improved in vivo diffusion tensor imaging of human cervical spinal cord. *Neuroimage* 2013; **67**: 64-76 [PMID: 23178538 DOI: 10.1016/j.neuroimage.2012.11.014]
- 17 **Yone K**, Sakou T, Yanase M, Ijiri K. Preoperative and postoperative magnetic resonance image evaluations of the spinal cord in cervical myelopathy. *Spine* (Phila Pa 1976) 1992; **17**: S388-S392 [PMID: 1440032 DOI: 10.1097/00007632-199210001-00008]
- 18 **Bohlman HH**. Cervical spondylosis and myelopathy. *Instr Course Lect* 1995; **44**: 81-97 [PMID: 7797895]
- 19 **Breig A**, Turnbull I, Hassler O. Effects of mechanical stresses on the spinal cord in cervical spondylosis. A study on fresh cadaver material. *J Neurosurg* 1966; **25**: 45-56 [PMID: 5947047]
- 20 **Firooznia H**, Benjamin VM, Pinto RS, Golimbu C, Rafii M, Leitman BS, McCauley DI. Calcification and ossification of posterior longitudinal ligament of spine: its role in secondary narrowing of spinal canal and cord compression. *N Y State J Med* 1982; **82**: 1193-1198 [PMID: 6813778]
- 21 **Mak KH**, Mak KL, Gwi-Mak E. Ossification of the ligamentum flavum in the cervicothoracic junction: case report on ossification found on both sides of the lamina. *Spine* (Phila Pa 1976) 2002; **27**: E11-E14 [PMID: 11805652 DOI: 10.1097/00007632-200201010-00027]
- 22 **Payne EE**, Spillane JD. The cervical spine; an anatomico-pathological study of 70 specimens (using a special technique) with particular reference to the problem of cervical spondylosis. *Brain* 1957; **80**: 571-596 [PMID: 13499761]
- 23 **Fehlings MG**, Skaf G. A review of the pathophysiology of cervical spondylotic myelopathy with insights for potential novel mechanisms drawn from traumatic spinal cord injury. *Spine* (Phila Pa 1976) 1998; **23**: 2730-2737 [PMID: 9879098 DOI: 10.1007/s00264-005-0002-x]
- 24 **Parke WW**. Correlative anatomy of cervical spondylotic myelopathy. *Spine* (Phila Pa 1976) 1988; **13**: 831-837 [PMID: 3194793 DOI: 10.1097/00007632-198807000-00023]
- 25 **Muthukumar N**. Ossification of the ligamentum flavum as a result of fluorosis causing myelopathy: report of two cases. *Neurosurgery* 2005; **56**: E622; discussion E622 [PMID: 15730589 DOI: 10.1227/01.NEU.0000154062.14313.6D]
- 26 **Green C**, Butler J, Eustace S, Poynton A, O'Byrne JM. Imaging modalities for cervical spondylotic stenosis and myelopathy. *Adv Orthop* 2012; **2012**: 908324 [PMID: 21991428 DOI: 10.1155/2012/908324]
- 27 **Ferreiro Perez A**, Garcia Isidro M, Ayerbe E, Castedo J, Jinkins JR. Evaluation of intervertebral disc herniation and hypermobile intersegmental instability in symptomatic adult patients undergoing recumbent and upright MRI of the cervical or lumbosacral spines. *Eur J Radiol* 2007; **62**: 444-448 [PMID: 17412542 DOI: 10.1016/j.ejrad.2006.12.007]
- 28 **Bednarik J**, Kadanka Z, Dusek L, Novotny O, Surelova D, Urbanek I, Prokes B. Presymptomatic spondylotic cervical cord compression. *Spine* (Phila Pa 1976) 2004; **29**: 2260-2269 [PMID: 15480138 DOI: 10.1007/s00586-008-0585-1]
- 29 **Basser PJ**, Pierpaoli C. Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. 1996. *J Magn Reson* 2011; **213**: 560-570 [PMID: 22152371 DOI: 10.1006/jmrb.1996.0086]
- 30 **Morio Y**, Nagashima H, Teshima R, Nawata K. Radiological pathogenesis of cervical myelopathy in 60 consecutive patients with cervical ossification of the posterior longitudinal ligament. *Spinal Cord* 1999; **37**: 853-857 [PMID: 10602528 DOI: 10.1038/sj.sc.3100940]
- 31 **Okawa A**, Nakamura I, Goto S, Moriya H, Nakamura Y, Ikegawa S. Mutation in Npps in a mouse model of ossification of the posterior longitudinal ligament of the spine. *Nat Genet* 1998; **19**: 271-273 [PMID: 9662402 DOI: 10.1038/956]
- 32 **Hashizume H**, Kawakami M, Nishi H, Tamaki T. Histochemical demonstration of nitric oxide in herniated lumbar discs. A clinical and animal model study. *Spine* (Phila Pa 1976) 1997; **22**: 1080-1084 [PMID: 9160465]
- 33 **Koshizuka Y**, Kawaguchi H, Ogata N, Ikeda T, Mabuchi A, Seichi A, Nakamura Y, Nakamura K, Ikegawa S. Nucleotide pyrophosphatase gene polymorphism associated with ossification of the posterior longitudinal ligament of the spine. *J Bone Miner Res* 2002; **17**: 138-144 [PMID: 11771660 DOI: 10.1359/jbmr.2002.17.1.138]
- 34 **Okano T**, Ishidou Y, Kato M, Imamura T, Yonemori K, Origuchi N, Matsunaga S, Yoshida H, ten Dijke P, Sakou T. Orthotopic ossification of the spinal ligaments of Zucker fatty rats: a possible animal model for ossification of the human posterior longitudinal ligament. *J Orthop Res* 1997; **15**: 820-829 [PMID: 9497806 DOI: 10.1002/jor.1100150606]
- 35 **Ono K**, Yonenobu K, Miyamoto S, Okada K. Pathology of ossification of the posterior longitudinal ligament and ligamentum flavum. *Clin Orthop Relat Res* 1999; **(359)**: 18-26 [PMID: 10078125 DOI: 10.1097/00003086-199902000-00003]
- 36 **Kalsi-Ryan S**, Karadimas SK, Fehlings MG. Cervical spondylotic myelopathy: the clinical phenomenon and the current pathobiology of an increasingly prevalent and devastating disorder. *Neuroscientist* 2013; **19**: 409-421 [PMID: 23204243 DOI: 10.1177/1073858412467377]
- 37 **Lee MJ**, Cassinelli EH, Riew KD. Prevalence of cervical spine stenosis. Anatomic study in cadavers. *J Bone Joint Surg Am* 2007; **89**: 376-380 [PMID: 17272453]
- 38 **Penning L**. Some aspects of plain radiography of the cervical spine in chronic myelopathy. *Neurology* 1962; **12**: 513-519 [PMID: 14485123 DOI: 10.1212/WNL.12.8.518]
- 39 **Murone I**. The importance of the sagittal diameters of the cervical spinal canal in relation to spondylosis and myelopathy. *J Bone Joint Surg Br* 1974; **56**: 30-36 [PMID: 4818851]
- 40 **Arnold JG**. The clinical manifestations of spondylochondrosis (spondylosis) of the cervical spine. *Ann Surg* 1955; **141**: 872-889 [PMID: 14377330]

- 41 **Penning L**, Wilmsink JT. Specificity of CT myelographic findings in cervical nerve root symptoms. *Neurosurg Rev* 1986; **9**: 99-101 [PMID: 3736907 DOI: 10.1007/BF01743058]
- 42 **Houser OW**, Onofrio BM, Miller GM, Folger WN, Smith PL. Cervical spondylotic stenosis and myelopathy: evaluation with computed tomographic myelography. *Mayo Clin Proc* 1994; **69**: 557-563 [PMID: 8189762 DOI: 10.1016/S0025-6196(12)62248-4]
- 43 **Ono K**, Ota H, Tada K, Yamamoto T. Cervical myelopathy secondary to multiple spondylotic protrusion: a clinico-pathologic study. *Spine* 1977; **2**: 109-125 [DOI: 10.1097/00007632-197706000-00004]
- 44 **Nakamura M**, Fujimura Y. Magnetic resonance imaging of the spinal cord in cervical ossification of the posterior longitudinal ligament. Can it predict surgical outcome? *Spine (Phila Pa 1976)* 1998; **23**: 38-40 [PMID: 9460150]
- 45 **Gundry CR**, Fritts HM. Magnetic resonance imaging of the musculoskeletal system. Part 8. The spine, section 2. *Clin Orthop Relat Res* 1997; **(343)**: 260-271 [PMID: 9345232]
- 46 **Abdulhadi MA**, Perno JR, Melhem ER, Nucifora PG. Characteristics of spondylotic myelopathy on 3D driven-equilibrium fast spin echo and 2D fast spin echo magnetic resonance imaging: a retrospective cross-sectional study. *PLoS One* 2014; **9**: e100964 [PMID: 25025170 DOI: 10.1371/journal.pone.0100964]
- 47 **White AA**, Panjabi MM. Biomechanical considerations in the surgical management of cervical spondylotic myelopathy. *Spine (Phila Pa 1976)* 1988; **13**: 856-860 [PMID: 3194796 DOI: 10.1097/00007632-198807000-00029]
- 48 **Kitahara Y**, Iida H, Tachibana S. Effect of spinal cord stretching due to head flexion on intramedullary pressure. *Neurol Med Chir (Tokyo)* 1995; **35**: 285-288 [PMID: 7623948 DOI: 10.2176/nmc.35.285]
- 49 **Koçak A**, Kiliç A, Nurlu G, Konan A, Kiliç K, Cirak B, Colak A. A new model for tethered cord syndrome: a biochemical, electrophysiological, and electron microscopic study. *Pediatr Neurosurg* 1997; **26**: 120-126 [PMID: 9419028 DOI: 10.1159/000121176]
- 50 **Yuan Q**, Dougherty L, Margulies SS. In vivo human cervical spinal cord deformation and displacement in flexion. *Spine (Phila Pa 1976)* 1998; **23**: 1677-1683 [PMID: 9704375 DOI: 10.1097/0007632-199808010-00012]
- 51 **Ichihara K**, Taguchi T, Sakuramoto I, Kawano S, Kawai S. Mechanism of the spinal cord injury and the cervical spondylotic myelopathy: new approach based on the mechanical features of the spinal cord white and gray matter. *J Neurosurg* 2003; **99**: 278-285 [PMID: 14563145 DOI: 10.3171/spi.2003.99.3.0278]
- 52 **Carlson GD**, Warden KE, Barbeau JM, Bahniuk E, Kutina-Nelson KL, Biro CL, Bohlman HH, LaManna JC. Viscoelastic relaxation and regional blood flow response to spinal cord compression and decompression. *Spine (Phila Pa 1976)* 1997; **22**: 1285-1291 [PMID: 9201829]
- 53 **Maxwell WL**, Domleo A, McColl G, Jafari SS, Graham DI. Post-acute alterations in the axonal cytoskeleton after traumatic axonal injury. *J Neurotrauma* 2003; **20**: 151-168 [PMID: 12675969 DOI: 10.1089/08977150360547071]
- 54 **Povlishock JT**. Traumatically induced axonal injury: pathogenesis and pathobiological implications. *Brain Pathol* 1992; **2**: 1-12 [PMID: 1341941]
- 55 **Iwasaki M**, Yamamoto T, Miyauchi A, Amano K, Yonenobu K. Cervical kyphosis: predictive factors for progression of kyphosis and myelopathy. *Spine (Phila Pa 1976)* 2002; **27**: 1419-1425 [PMID: 12131739]
- 56 **Muhle C**, Metzner J, Weinert D, Schön R, Rautenberg E, Falliner A, Brinkmann G, Mehdorn HM, Heller M, Resnick D. Kinematic MR imaging in surgical management of cervical disc disease, spondylosis and spondylotic myelopathy. *Acta Radiol* 1999; **40**: 146-153 [PMID: 10080726 DOI: 10.3109/02841859909177730]
- 57 **Yonenobu K**, Okada K, Fuji T, Fujiwara K, Yamashita K, Ono K. Causes of neurologic deterioration following surgical treatment of cervical myelopathy. *Spine (Phila Pa 1976)* 1986; **11**: 818-823 [PMID: 3810299 DOI: 10.1097/00007632-198610000-00016]
- 58 **Bunge RP**, Puckett WR, Becerra JL, Marcillo A, Quencer RM. Observations on the pathology of human spinal cord injury. A review and classification of 22 new cases with details from a case of chronic cord compression with extensive focal demyelination. *Adv Neurol* 1993; **59**: 75-89 [PMID: 8420126]
- 59 **Agrawal SK**, Fehlings MG. Mechanisms of secondary injury to spinal cord axons in vitro: role of Na⁺, Na⁽⁺⁾-K⁽⁺⁾-ATPase, the Na⁽⁺⁾-H⁺ exchanger, and the Na⁽⁺⁾-Ca²⁺ exchanger. *J Neurosci* 1996; **16**: 545-552 [PMID: 8551338]
- 60 **Agrawal SK**, Fehlings MG. Role of NMDA and non-NMDA ionotropic glutamate receptors in traumatic spinal cord axonal injury. *J Neurosci* 1997; **17**: 1055-1063 [PMID: 8994060]
- 61 **Crowe MJ**, Bresnahan JC, Shuman SL, Masters JN, Beattie MS. Apoptosis and delayed degeneration after spinal cord injury in rats and monkeys. *Nat Med* 1997; **3**: 73-76 [PMID: 8986744 DOI: 10.1038/nm0197-73]
- 62 **Delamarter RB**, Sherman J, Carr JB. Pathophysiology of spinal cord injury. Recovery after immediate and delayed decompression. *J Bone Joint Surg Am* 1995; **77**: 1042-1049 [PMID: 7608226]
- 63 **Fehlings MG**, Agrawal S. Role of sodium in the pathophysiology of secondary spinal cord injury. *Spine (Phila Pa 1976)* 1995; **20**: 2187-2191 [PMID: 8545710 DOI: 10.1097/00007632-199510001-00002]
- 64 **Fehlings MG**, Tator CH. The relationships among the severity of spinal cord injury, residual neurological function, axon counts, and counts of retrogradely labeled neurons after experimental spinal cord injury. *Exp Neurol* 1995; **132**: 220-228 [PMID: 7789460 DOI: 10.1016/0014-4886(95)90027-6]
- 65 **Tator CH**, Fehlings MG. Review of the secondary injury theory of acute spinal cord trauma with emphasis on vascular mechanisms. *J Neurosurg* 1991; **75**: 15-26 [PMID: 2045903 DOI: 10.3171/jns.1991.75.1.0015]
- 66 **Gooding MR**, Wilson CB, Hoff JT. Experimental cervical myelopathy. Effects of ischemia and compression of the canine cervical spinal cord. *J Neurosurg* 1975; **43**: 9-17 [PMID: 1141988]
- 67 **Baron EM**, Young WF. Cervical spondylotic myelopathy: a brief review of its pathophysiology, clinical course, and diagnosis. *Neurosurgery* 2007; **60**: S35-S41 [PMID: 17204884 DOI: 10.1227/01.NEU.0000215383.64386.82]
- 68 **Ogino H**, Tada K, Okada K, Yonenobu K, Yamamoto T, Ono K, Namiki H. Canal diameter, anteroposterior compression ratio, and spondylotic myelopathy of the cervical spine. *Spine (Phila Pa 1976)* 1983; **8**: 1-15 [PMID: 6867846 DOI: 10.1097/00007632-198301000-00001]
- 69 **Gooding MR**. Pathogenesis of myelopathy in cervical spondylosis. *Lancet* 1974; **2**: 1180-1181 [PMID: 4139596]
- 70 **al-Mefty O**, Harkey HL, Marawi I, Haines DE, Peeler DF, Wilner HI, Smith RR, Holaday HR, Haining JL, Russell WF. Experimental chronic compressive cervical myelopathy. *J Neurosurg* 1993; **79**: 550-561 [PMID: 8410225]
- 71 **Doppman JL**. The mechanism of ischemia in anteroposterior compression of the spinal cord 1975. *Invest Radiol* 1990; **25**: 444-452 [PMID: 2185194]
- 72 **Shuman SL**, Bresnahan JC, Beattie MS. Apoptosis of microglia and oligodendrocytes after spinal cord contusion in rats. *J Neurosci Res* 1997; **50**: 798-808 [PMID: 9418967]
- 73 **Li Y**, Field PM, Raisman G. Death of oligodendrocytes and microglial phagocytosis of myelin precede immigration of Schwann cells into the spinal cord. *J Neurocytol* 1999; **28**: 417-427 [PMID: 10739580 DOI: 10.1023/A: 1007026001189]
- 74 **Gledhill RF**, Harrison BM, McDonald WI. Demyelination and remyelination after acute spinal cord compression. *Exp Neurol* 1973; **38**: 472-487 [PMID: 4696114 DOI: 10.1016/0014-4886(73)90169-6]
- 75 **Ohshio I**, Hatayama A, Kaneda K, Takahara M, Nagashima K. Correlation between histopathologic features and magnetic resonance images of spinal cord lesions. *Spine (Phila Pa 1976)* 1993; **18**: 1140-1149 [PMID: 8362319]
- 76 **Uchida K**, Nakajima H, Sato R, Kokubo Y, Yayama T, Kobayashi S, Baba H. Multivariate analysis of the neurological outcome of surgery for cervical compressive myelopathy. *J Orthop Sci* 2005;

- 10: 564-573 [PMID: 16307181 DOI: 10.1007/s00776-005-0953-1]
- 77 **Choi DW.** Excitotoxic cell death. *J Neurobiol* 1992; **23**: 1261-1276 [PMID: 1361523 DOI: 10.1002/neu.480230915]
- 78 **Shaw PJ,** Ince PG. Glutamate, excitotoxicity and amyotrophic lateral sclerosis. *J Neurol* 1997; **244** Suppl 2: S3-14 [PMID: 9178165 DOI: 10.1007/BF03160574]
- 79 **Schrank B,** Götz R, Gunnarsen JM, Ure JM, Toyka KV, Smith AG, Sendtner M. Inactivation of the survival motor neuron gene, a candidate gene for human spinal muscular atrophy, leads to massive cell death in early mouse embryos. *Proc Natl Acad Sci USA* 1997; **94**: 9920-9925 [PMID: 9275227]
- 80 **Kato H,** Kanellopoulos GK, Matsuo S, Wu YJ, Jacquin MF, Hsu CY, Kouchoukos NT, Choi DW. Neuronal apoptosis and necrosis following spinal cord ischemia in the rat. *Exp Neurol* 1997; **148**: 464-474 [PMID: 9417826 DOI: 10.1006/exnr.1997.6707]
- 81 **Lipton SA.** Molecular mechanisms of trauma-induced neuronal degeneration. *Curr Opin Neurol Neurosurg* 1993; **6**: 588-596 [PMID: 8400474]
- 82 **Blight AR.** Delayed demyelination and macrophage invasion: a candidate for secondary cell damage in spinal cord injury. *Cent Nerv Syst Trauma* 1985; **2**: 299-315 [PMID: 3836014 DOI: 10.1089/cns.1985.2.299]
- 83 **Villa PG,** Henzel WJ, Sensenbrenner M, Henderson CE, Pettmann B. Calpain inhibitors, but not caspase inhibitors, prevent actin proteolysis and DNA fragmentation during apoptosis. *J Cell Sci* 1998; **111** (Pt 6): 713-722 [PMID: 9472000]
- 84 **Pérez-García MT,** Chiamvimonvat N, Ranjan R, Balsler JR, Tomaselli GF, Marban E. Mechanisms of sodium/calcium selectivity in sodium channels probed by cysteine mutagenesis and sulfhydryl modification. *Biophys J* 1997; **72**: 989-996 [PMID: 9138597 DOI: 10.1016/S0006-3495(97)78751-4]
- 85 **Shaked I,** Porat Z, Gersner R, Kipnis J, Schwartz M. Early activation of microglia as antigen-presenting cells correlates with T cell-mediated protection and repair of the injured central nervous system. *J Neuroimmunol* 2004; **146**: 84-93 [PMID: 14698850 DOI: 10.1016/j.jneuroim.2003.10.049]
- 86 **Beattie MS,** Manley GT. Tight squeeze, slow burn: inflammation and the aetiology of cervical myelopathy. *Brain* 2011; **134**: 1259-1261 [PMID: 21596766 DOI: 10.1093/brain/awr088]
- 87 **Sadhu A,** Ahn NU. Cocaine use and surgical outcomes of cervical spondylotic myelopathy: a retrospective study. *Orthopedics* 2012; **35**: e1640-e1643 [PMID: 23127457 DOI: 10.3928/01477447-2012-1023-23]
- 88 **Wang ZC,** Shi JG, Chen XS, Xu GH, Li LJ, Jia LS. The role of smoking status and collagen IX polymorphisms in the susceptibility to cervical spondylotic myelopathy. *Genet Mol Res* 2012; **11**: 1238-1244 [PMID: 22614351 DOI: 10.4238/2012.May.9.2]
- 89 **Akmal M,** Kesani A, Anand B, Singh A, Wiseman M, Goodship A. Effect of nicotine on spinal disc cells: a cellular mechanism for disc degeneration. *Spine (Phila Pa 1976)* 2004; **29**: 568-575 [PMID: 15129075 DOI: 10.1097/01.BRS.0000101422.36419.D8]
- 90 **Bull J,** el Gammal T, Popham M. A possible genetic factor in cervical spondylosis. *Br J Radiol* 1969; **42**: 9-16 [PMID: 5782795 DOI: 10.1259/0007-1285-42-493-9]
- 91 **Sambrook PN,** MacGregor AJ, Spector TD. Genetic influences on cervical and lumbar disc degeneration: a magnetic resonance imaging study in twins. *Arthritis Rheum* 1999; **42**: 366-372 [PMID: 10025932 DOI: 10.1002/1529-0131(199902)42: 2<366::AID-ANR20>3.0.CO;2-6]
- 92 **Yoo K,** Origiano TC. Familial cervical spondylosis. Case report. *J Neurosurg* 1998; **89**: 139-141 [PMID: 9647185 DOI: 10.3171/jns.1998.89.1.0139]
- 93 **Mukerji N,** Todd NV. Cervical myelopathy in rheumatoid arthritis. *Neurol Res Int* 2011; **2011**: 153628 [PMID: 22203899 DOI: 10.1155/2011/153628]
- 94 **Falcón-Ramírez E,** Casas-Avila L, Miranda A, Diez P, Castro C, Rubio J, Gómez R, Valdés-Flores M. Sp1 polymorphism in collagen I $\alpha 1$ gene is associated with osteoporosis in lumbar spine of Mexican women. *Mol Biol Rep* 2011; **38**: 2987-2992 [PMID: 20146006 DOI: 10.1007/s11033-010-9963-y]
- 95 **Lucas SR,** Bass CR, Crandall JR, Kent RW, Shen FH, Salzar RS. Viscoelastic and failure properties of spine ligament collagen fascicles. *Biomech Model Mechanobiol* 2009; **8**: 487-498 [PMID: 19308471 DOI: 10.1007/s10237-009-0152-7]
- 96 **Zhu Y,** Wu JJ, Weis MA, Mirza SK, Eyre DR. Type IX collagen neo-deposition in degenerative discs of surgical patients whether genotyped plus or minus for COL9 risk alleles. *Spine (Phila Pa 1976)* 2011; **36**: 2031-2038 [PMID: 21311409 DOI: 10.1097/BRS.0b013e3181ffdd61]
- 97 **Mukerji SS,** Parmar H, Ibrahim M, Bradford C. An unusual cause of recurrent pediatric neck abscess: pyriform sinus fistula. *Clin Imaging* 2007; **31**: 349-351 [PMID: 17825745 DOI: 10.1016/j.clinimag.2007.03.001]
- 98 **Uchida K,** Nakajima H, Yayama T, Kobayashi S, Shimada S, Tsuchida T, Okazawa H, Mwaka E, Baba H. High-resolution magnetic resonance imaging and 18FDG-PET findings of the cervical spinal cord before and after decompressive surgery in patients with compressive myelopathy. *Spine (Phila Pa 1976)* 2009; **34**: 1185-1191 [PMID: 19407675 DOI: 10.1097/BRS.0b013e31819e2919]
- 99 **Uchida K,** Kobayashi S, Yayama T, Kokubo Y, Nakajima H, Kakuyama M, Sadato N, Tsuchida T, Yonekura Y, Baba H. Metabolic neuroimaging of the cervical spinal cord in patients with compressive myelopathy: a high-resolution positron emission tomography study. *J Neurosurg Spine* 2004; **1**: 72-79 [PMID: 15291024 DOI: 10.3171/spi.2004.1.1.0072]

P- Reviewer: Aota Y, Mori K

S- Editor: Ji FF L- Editor: A E- Editor: Li D



Role of negative pressure wound therapy in total hip and knee arthroplasty

Marcelo BP Siqueira, Deepak Ramanathan, Alison K Klika, Carlos A Higuera, Wael K Barsoum

Marcelo BP Siqueira, Deepak Ramanathan, Alison K Klika, Carlos A Higuera, Wael K Barsoum, Department of Orthopaedic Surgery, Orthopaedic and Rheumatologic Institute, Cleveland Clinic Foundation, Cleveland, OH 44195, United States

Author contributions: Siqueira MBP and Ramanathan D reviewed the literature for this minireview and wrote the manuscript; Klika AK, Higuera CA and Barsoum WK edited the manuscript.

Conflict-of-interest statement: No financial support was received for this study. One author Carlos A Higuera has received research support funding from Stryker and KCI outside the submitted work; One author Carlos A Higuera lists the following relevant financial activities outside of this work and/or any other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, this manuscript; in the amount of USD 100001-USD 1000000 from Stryker and KCI; One author Wael K Barsoum has received research support from grants from Stryker, Zimmer, personal fees from Shukla Medical, personal fees from Wright Medical Technology, personal fees from Exactech, personal fees from KEF Healthcare, other from OtisMed Corporation, other from Custom Orthopaedic Solution, other from iVHR, grants from DJO, grants from Active Implants, grants from The Medicines Company, grants from State of Ohio, grants from Orthovita, grants from CoolSystems, grants from Orthopaedic Research and Education Foundation, grants from Salient Surgical Technologies, outside the submitted work; One author Wael K Barsoum lists the following relevant financial activities outside of this work and/or any other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, this manuscript; in the amount of USD 100001-USD 1000000 from the above institutions. None of the other authors have any conflicts of interest to report.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Alison K Klika, MS, Research Program Manager, Department of Orthopaedic Surgery, Orthopaedic and Rheumatologic Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. klikaa@ccf.org
Telephone: +1-216-4444954
Fax: +1-216-4456255

Received: May 24, 2015
Peer-review started: May 25, 2015
First decision: August 16, 2015
Revised: October 2, 2015
Accepted: November 17, 2015
Article in press: November 25, 2015
Published online: January 18, 2016

Abstract

Negative-pressure wound therapy (NPWT) has been a successful modality of wound management which is in widespread use in several surgical fields. The main mechanisms of action thought to play a role in enhancing wound healing and preventing surgical site infection are macrodeformation and microdeformation of the wound bed, fluid removal, and stabilization of the wound environment. Due to the devastating consequences of infection in the setting of joint arthroplasty, there has been some interest in the use of NPWT following total hip arthroplasty and total knee arthroplasty. However, there is still a scarcity of data reporting on the use of NPWT within this field and most studies are limited by small sample sizes, high variability of clinical settings and end-points. There is little evidence to support the use of NPWT as an adjunctive treatment for surgical wound drainage, and for this reason surgical intervention should not be delayed when indicated. The prophylactic use of NPWT after arthroplasty in patients that are at high risk for postoperative wound drainage appears to have the strongest clinical evidence. Several clinical trials

including single-use NPWT devices for this purpose are currently in progress and this may soon be incorporated in clinical guidelines as a mean to prevent periprosthetic joint infections.

Key words: Negative-pressure wound therapy; Vacuum-assisted closure; Total knee replacement; Total hip replacement; Prosthesis-related infections

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The application of negative pressure wound therapy (NPWT) in arthroplasty has generated much interest. Its proposed mechanisms of action include macrodeformation and microdeformation of the wound bed, fluid removal, and stabilization of the wound environment. There is little evidence to support the use of NPWT as an adjunctive treatment for surgical wound drainage. However, there appears to be strong clinical evidence for the prophylactic use of NPWT after arthroplasty in patients that are at high risk for postoperative wound drainage. Several clinical trials involving single-use NPWT devices for this purpose are currently in progress.

Siqueira MBP, Ramanathan D, Klika AK, Higuera CA, Barsoum WK. Role of negative pressure wound therapy in total hip and knee arthroplasty. *World J Orthop* 2016; 7(1): 30-37 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/30.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.30>

INTRODUCTION

The use of negative pressure for wound healing, also referred to as vacuum-assisted closure, is a well-established practice that dates back to the 1940s^[1-3]. While this technique was originally intended for flaps, skin grafts, and radical neck and groin dissection, its success has led to a rapid expansion of indications with over 700 articles describing its use^[4]. Current evidence-based indications for the use of negative pressure on wound healing are broad and include chronic, acute, traumatic, subacute and dehisced wounds, partial-thickness burns, ulcers (such as diabetic or pressure), flaps and grafts^[4-12].

The rationale behind the use of subatmospheric pressure for wound healing is based upon a wide array of mechanisms that ultimately result in wound contraction, mechanical stimulation of epithelial growth, and prevention of fluid collection, drainage and bacterial growth^[13,14]. Despite the extensive literature, there is considerable controversy regarding its efficiency and applicability in certain clinical situations. A recent systematic review identified thirteen randomized clinical trials studying the use of negative pressure wound therapy (NPWT) and suggested that there is still little evidence

to support its use in the treatment of acute and chronic wounds^[15].

Periprosthetic joint infection (PJI) can be a devastating complication after joint arthroplasty. With the potential to not only treat but also prevent wound complications, there has been some interest surrounding the use of NPWT in the setting of joint arthroplasty. Patel *et al.*^[16] have shown that specific patient characteristics are associated with prolonged wound drainage following total hip arthroplasty (THA) and total knee arthroplasty (TKA). Prolonged wound drainage (*i.e.*, greater than five days postoperative) puts a patient at 12.7 times higher risk of PJI^[17]. The ability to preoperatively determine candidates at higher risk for prolonged wound drainage (and hence, PJI) would enable the surgeon to consider NPWT in those arthroplasty patients who could benefit most from its use. To date, however, there are no specific guidelines, indications, or reviews on the use of NPWT after TKA and THA. This review will provide a brief introduction on the history and rationale of NPWT, its basic mechanisms of action, current evidence in the field of TKA and THA, contraindications, complications, risk factors and perspectives for future research in this area.

BRIEF HISTORY AND RATIONALE OF NPWT

Despite meticulous hemostasis and tissue-handling techniques, any operation that requires separation of tissue planes and extensive tissue manipulation will cause some amount of fluid collection within the surgical wound. Fluid build-up can be detrimental to wound healing as it impedes normal blood flow and eventually leads to the formation of dense fibrous tissue. Prior to NPWT, common strategies to deal with this problem included devices such as Penrose drains and pressure dressings^[18]. Numerous cases of debilitated patients with chronic, dehisced, and often infected wounds not amenable to closure led to the implementation of subatmospheric pressure systems^[19]. This treatment modality provided not only complete coverage of the wound, but also constant interstitial fluid removal and mechanical stimulation of surrounding tissues. Sheppard^[1] was the first to report the use of sealed drainage over surface wounds. However, the application of continuous subatmospheric pressure to this drainage system was first described by Raffi^[2]. While initially intended for chronic, non-healing wounds on debilitated patients, the indications for NPWT expanded to include subacute and acute wounds^[20-24].

There are five basic components to any NPWT system: The foam, tube, drapes, pump and canister. The foam is placed in direct contact with the wound and can be tailored to its specific geometry. Typically, the foam is made of polyurethane ether and is composed of highly interconnected cells of size ranging between 400-600 μm in diameter^[25,26]. The so-called open-pore foam allows the pressure to be evenly distributed throughout

its entire surface. A non-collapsible tube is embedded in the foam and connected to a vacuum pump. The ideal pressure applied by the pump may vary according to the fragility of the surrounding tissues but optimal granulation tissue formation has been reported with a subatmospheric pressure of 125 mmHg^[27]. Semio-occlusive adhesive drapes cover the surface of the wound containing the foam and these ensure an airtight seal. Finally, the proximal end of the tube leads to a canister that functions as a remote storage recipient for effluent fluid^[19].

The first commercially available device that achieved widespread usage, in the early 1990s, was the Vacuum-assisted wound closure device and technology (V.A.C.) [Kinetic Concepts Inc. (KCI), San Antonio, TX]. Landmark publications by Argenta *et al.*^[19] detailing the basic mechanism of NPWT and Morykwas *et al.*^[14] describing its clinical utility contributed to increasing acceptance of the NPWT. Since then, significant advances have been made to the device to improve safety and functionality. First, the incorporation of computerized alarm systems made it possible to detect inadequate seal, excessive fluid output and bleeding. Second, the development of compact, lightweight devices allowed patients to remain ambulatory throughout the duration of treatment^[28]. Third, newer models also allow the instillation of fluids without loss of negative pressure in an attempt to continuously remove particulate and bacterial matter. These have been particularly useful in the setting of deep, contaminated wounds^[29,30]. The recent use of silver coated foam is intended to provide a local antibacterial effect^[31,32].

There is some concern regarding the overall quality and conflict of interest associated with the published studies supporting the use of NPWT in various clinical settings. One contributor to this problem is the heterogeneity of published articles in terms of wound types, comparisons and outcome variables^[15]. Conflict of interest in NPWT-related research is also a matter of concern since the main research sponsors are the two leading device manufacturers. Despite the great commercial success, there is still a lack of data supporting the benefits of NPWT on wound closure^[24].

MECHANISMS OF ACTION

The application of NPWT on wound beds has direct and indirect effects on wound healing. There are four main direct mechanisms by which NPWT has been suggested to work: (1) macrodeformation; (2) microdeformation; (3) fluid removal; and (4) stabilization of the environment^[33]. Numerous indirect effects of NPWT on wound healing have also been proposed, including the modulation of inflammation^[34], angiogenesis^[35], granulation tissue formation^[36,37], peripheral nerve response^[38,39] and alteration in bioburden^[7]. This section will focus mainly on the four direct mechanisms as they are more broadly studied and widely accepted.

The concept of macrodeformation involves the con-

traction of the foam once subatmospheric pressure is applied. Foam contraction exerts centripetal traction at the wound-foam interface resulting in approximation of the edges and decreased wound surface area^[40]. The increased pressure applied to the tissue below the wound bed also contributes to the compression of capillaries, creating a localized decrease in perfusion. As a result, local upregulation of hypoxia-inducible growth factor production, including vascular endothelial growth factor, stimulates directionalized vessel sprouting towards the wound^[33]. The end result of macrodeformation of the wound bed is thus a decrease in wound surface area and increased local vascularity.

When exposed to subatmospheric pressure, the porous surface of the foam induces microdeformations in the underlying tissue by creating an undulated surface of the wound bed^[41]. Cell deformation leads to cytoskeletal stretch which in turn provides an independent stimulus for cell proliferation, migration, and differentiation^[42]. As a consequence, the conformational changes induced in the surface of the wound by the porous surface of the foam ultimately result in increased epithelial cell proliferation as compared to normal occlusive dressings^[40].

Fluid removal is an essential mechanism by which NPWT relieves the compressive effect of extracellular fluid on surrounding tissues^[43] and clears the wound from toxins, exudates and bacteria^[44]. Indirectly, this also reduces the amount of fluid that must be cleared by the lymphatics and induces a local increase in lymphatic density^[45]. Less extracellular fluid build-up also translates into decreased capillary compression and increased tissue perfusion^[43].

Finally, NPWT dressings have the ability to transform an open wound into a closed wound. The semiocclusive drapes covering the foam and surrounding skin maintain thermal stability, prevent evaporative water losses^[46], stabilize osmotic and oncotic gradients at the wound surface^[47] and reduce the risk of external contamination^[48]. The semiocclusive aspect of the drapes also allows for limited permeability to vapor and other gases in order to maintain a moist wound environment^[46].

CURRENT EVIDENCE IN HIP AND KNEE ARTHROPLASTY

The use of NPWT was pioneered in plastic surgery and subsequently adopted by other surgical fields, including vascular, cardiothoracic and abdominal surgery. In orthopaedic surgery, there is limited literature on the use of NPWT. In a systematic review, Karlakki *et al.*^[49] identified 9 studies reporting the use of NPWT in orthopaedic surgery, five of which were Randomized controlled trials (RCTs). There is an even greater scarcity of published studies concerning the use of NPWT in adult reconstructive surgery. In this review, we identified eight studies reporting on the use of NPWT on either THA or TKA (Table 1).

Table 1 Literature on negative pressure wound therapy on hip and knee arthroplasty

Ref.	Origin	Type	Indication	Device, negative pressure delivery	Length of use	Results	Conflict of Interest
Gomoll <i>et al.</i> ^[50]	United States	Case series	Revision THA with history of multiple revisions (<i>n</i> = 1 NPWT), hemiarthroplasty with bladder/bowel incontinence (<i>n</i> = 1 NPWT)	V.A.C. [®] , 75 mmHg	3 d (average)	Incisions noted to be well healed at a minimum of 3 mo	No
Kirr <i>et al.</i> ^[51]	Germany	Case series	I and D for acute hip (<i>n</i> = 3 NPWT) and knee PJI (<i>n</i> = 2 NPWT)	V.A.C. [®] instill system with antibiotic instillation, amount of pressure delivery N/A	15.2 d (average)	Eradication of infection in all cases, complete wound healing achieved in 10-14 d	N/A
Lehner <i>et al.</i> ^[52]	Germany	Case series	I and D for acute hip (<i>n</i> = 2 NPWT), and knee PJI (<i>n</i> = 1 NPWT)	V.A.C. [®] instill system with antiseptic solution, 100-150 mmHg	6 d (average)	Retention of all 3 implants with no further signs of infection at a minimum of 8 wk	N/A
Kelm <i>et al.</i> ^[53]	Germany	Case series	I and D for acute hip PJI (<i>n</i> = 28 NPWT)	Periprosthetic placement of V.A.C. [®] , 200 mmHg for 72 h, and 150 mmHg	6 d	Infection eradication in 26/28 cases with implant retention at a minimum of 12 mo	No
Howell <i>et al.</i> ^[54]	United States	RCT	Primary THA with increased risk for postoperative drainage (<i>n</i> = 24 NPWT <i>vs</i> <i>n</i> = 36)	V.A.C. [®] , 125 mmHg	2 d	No difference in days to dry wound; 1 PJI in each group. Study stopped because of skin blisters in 63% of patients in NPWT arm	Yes
Pachowsky <i>et al.</i> ^[55]	Germany	RCT	Primary THA for OA (<i>n</i> = 9 NPWT <i>vs</i> <i>n</i> = 10)	Prevena [™] , 125 mmHg	5 d	Decreased seroma development in NPWT group (<i>P</i> = 0.021)	Yes
Hansen <i>et al.</i> ^[56]	United States	Retrospective cohort	Persistent wound drainage at POD 3 to 4 after primary THA (<i>n</i> = 86 NPWT) and revision THA (<i>n</i> = 23 NPWT)	V.A.C. [®] , 125 mmHg	24-48 h	83 (76%) had no further surgery, 26 (24%) had further surgery. No NPWT-related complications	No
Pauser <i>et al.</i> ^[57]	Germany	RCT	Hemiarthroplasty after femoral neck fracture (<i>n</i> = 11 NPWT <i>vs</i> <i>n</i> = 10)	Prevena [™] , 125 mmHg	5 d	NPWT group had fewer dressing changes, less days of wound secretion, less wound care time, and less dressing material used (<i>P</i> < 0.05 for all)	Yes

V.A.C.[®]: Vacuum assisted closure system (KCI, San Antonio, TX); Prevena[™]: Prevena incision management system (KCI, San Antonio, TX); THA: Total hip arthroplasty; TKA: Total knee arthroplasty; NPWT: Negative pressure wound therapy; PJI: Periprosthetic joint infection; I and D: Incision and debridement; RCT: Randomized controlled trial; OA: Osteoarthritis; N/A: Not available; KCI: Kinetic Concepts Inc.; POD: Post-operative day.

Gomoll *et al.*^[50] reported their experience in five cases in which NPWT was used as a postoperative dressing for primarily closed incisions. Indications included either a high likelihood of prolonged wound drainage or procedures performed in areas prone to postoperative swelling. This was among the first reported prophylactic use of NPWT in orthopaedic surgery. Of the five cases, two involved hip reconstruction. In one patient, NPWT was used because of large dead space and extensive soft tissue dissection. In the other case, NPWT was used because of the increased risk of contamination secondary to bladder and bowel incontinence. Treatment duration averaged three days and negative pressure was set at 75 mmHg. At three months post-operatively, the incisions were well-healed without complications. The remaining three cases involved the use of NPWT after open reduction and internal fixation for comminuted pilon, intertrochanteric, and subtrochanteric fractures which are not discussed here.

A series of papers originating from Germany reported on the therapeutic use of NPWT after acute PJI. Kirr *et al.*^[51] used a newer model of NPWT in which the direct instillation of fluids to the wound is made possible without the loss of negative pressure. The device was used on five cases after irrigation and débridement (I and D) for acute PJI in which the wound was left open. Fluids used for instillation included a local antibiotic (bacitracin with neomycin sulfate) and an antiseptic solution (polihexanide). Complete wound healing was achieved in all five patients after fourteen days of therapy. In a similar study, Lehner and Bernd^[52] used the same device with instillation therapy to treat three cases of acute hip or knee PJI. Instillation was made with only a solution of polihexanide. At eight weeks, retention of all three implants was successfully achieved. Lastly, Kelm *et al.*^[53] reported on 28 cases of acute hip PJI managed with I and D followed by an internal use of NPWT. This was the first study to report the placement of the foam either periprosthetically or into the resection cavity with an outgoing transcatheter tube. The wound was closed and inflammation parameters monitored. After a mean duration of nine days, surgical removal of the foam was performed. The foam was exchanged in cases in which there were macroscopic signs of persistence of the

infection. At a mean follow-up of 36 mo, eradication of infection was achieved in 26 out of the 28 cases. These three preliminary case series suggest a potential role for NPWT in the treatment of PJI, which requires further testing with large scale, controlled studies to support this practice.

Howell *et al.*^[54] conducted a RCT to establish the benefit of prophylactic NPWT after TKA in patients at high risk for prolonged wound drainage. High risk was defined as body mass index > 30 and the use of enoxaparin sodium for deep venous thrombosis prophylaxis. The trial was prematurely interrupted when a total of 60 knees were enrolled and a significant difference in blister formation was detected between the NPWT group and the control group. Among the 24 knees in the NPWT group, 15 (63%) developed linear blisters at the edges of the polyurethane ether foam, whereas only three out of 36 knees in the control group (12%) developed blisters. There was no difference in time to a dry wound or incidence of PJI between the two groups. In order to address the issue of blistering, a single fine-meshed, non-adherent film was recommended for use over unprotected skin in order to avoid direct contact with the foam^[54]. This has already been incorporated in single-use, disposable devices such as Prevena™ (KCI, San Antonio, Texas) and PICO™ (Smith and Nephew, Hull, United Kingdom) and the blistering complication has not been reported in subsequent studies.

Another RCT evaluating the prophylactic use of NPWT for wound complications was conducted by Pachowsky *et al.*^[55]. Inclusion criteria included normal-risk THA for osteoarthritis, with nine patients receiving a single use NPWT device for five days and ten patients receiving a standard occlusive dressing. The novelty of this study was its primary end-point: The development of post-operative seromas as detected through ultrasound measurements. On post-operative day ten, a seroma was present in 44% of patients in the NPWT group as compared to 90% in the control group, with a significantly decreased seroma volume in the NPWT group (1.97 mL vs 5.08 mL, $P = 0.021$). Although reduction of postoperative seromas may potentially lead to increased blood flow and better apposition of the wound edges, there are no data to suggest that this is specifically linked to decreased rates of PJI and to justify the use of NPWT in normal-risk patients.

Hansen *et al.*^[56] investigated the therapeutic use of NPWT for persistent incisional drainage after primary and revision THA. Indication for NPWT was persistent wound drainage at postoperative days 3 to 4. Interestingly, 83 patients (76%) had complete resolution of wound drainage without further surgical intervention. Of the 26 patients who required further intervention despite NPWT, 23 (88%) had complete resolution of drainage after a single I and D. This study was the first in the field of reconstructive surgery to attempt NPWT first instead of I and D. Furthermore, it was reported that failed therapy with NPWT did not compromise the results of a

subsequent I and D. Even though this was a retrospective study, it provided important data as to the value of NPWT as primary therapy for early wound drainage.

Lastly, Pauser *et al.*^[57] conducted a RCT studying the prophylactic use of NPWT after hemiarthroplasties for femoral neck fractures. Eleven patients were randomized to the NPWT group and ten patients to a control group (occlusive dressing). The end-points chosen for analysis were the number of dressing changes ($P < 0.0001$), days of wound secretion ($P = 0.0005$) and wound care time ($P < 0.0001$). Statistical significance was achieved in all three end-points favoring the NPWT group. Furthermore, there was a decreased incidence of seromas in the NPWT group (36% vs 80%). Despite the limited sample size, this study attempted to show not only the main benefits of NPWT in terms of wound healing, but also secondary gains such as less time spent by health care professionals and less consumption of wound care resources.

Overall, there is a clear lack of high-ranking scientific evidence in the field of adult reconstructive surgery concerning the use of NPWT. Studies are limited by a high variability of clinical settings and small sample sizes. The prophylactic use of NPWT after arthroplasty in high risk candidates seems to have the strongest clinical evidence^[54,56,58]. The use of NPWT as an adjunctive therapy for acute PJI after I and D is only supported by small case series^[51-53]. Finally, the use of NPWT as the main therapy for postoperative wound drainage is supported by a single retrospective study^[56].

CONTRA-INDICATIONS, COMPLICATIONS AND RISK FACTORS

According to the Food and Drug Administration (FDA), due to the lack of appropriate studies, NPWT should be contraindicated in the following scenarios: (1) necrotic tissue or eschar present; (2) untreated osteomyelitis; (3) unexplored fistulas; (4) malignancy in the wound; and (5) exposed vasculature, nerves, anastomotic sites or organs^[58]. These guidelines were based on two major concerns: (1) the inability of NPWT to replace surgical treatment when this is formally indicated; and (2) the mechanical strain that sub-atmospheric pressure can place upon fragile tissues.

Despite the rapid expansion in the use of NPWT across various clinical settings, the reported complication rates are surprisingly low. The most worrisome and potentially lethal complication has been exsanguination. Four fatal exsanguinations have been reported with use of NPWT and these occurred when the tube was attached to wall suction^[59]. This practice is now strongly condemned and the use of safety alarms for excessive fluid drainage has been incorporated to NPWT devices. Safety alarms are also designed to detect air leaks, as this has been shown to increase wound size due to skin dehydration^[27]. Fatal toxic shock syndrome has been reported in two cases, both of which had a purportedly blockage in the drainage system^[60]. Retention

of foam within the wound, particularly when multiple, small fragments of foam were used, is also a known complication^[33]. Lastly, blistering has been a minor complication in most studies within orthopaedic surgery, except for one^[54]. This problem has largely been resolved with the addition of a protective adhesive layer between the foam and skin.

Patient-related risk factors that demand special attention when considering NPWT are: (1) high risk of bleeding and hemorrhage; (2) use of anticoagulants or platelet aggregation inhibitors; (3) patients with friable or infected blood vessels, vascular anastomosis, infected wounds, osteomyelitis, exposed organs, vessels, nerves, tendons, and ligaments, sharp edges in the wound, spinal cord injury, enteric fistulas; (4) patients requiring magnetic resonance imaging, hyperbaric chamber, defibrillation; (5) patient size and weight (increased dead space); (6) proximity to vagus nerve (with risk of bradycardia); (7) circumferential dressing application; and (8) mode of therapy (intermittent vs continuous negative pressure)^[58]. The FDA report also stresses that the vast majority of adverse events and deaths related to NPWT has occurred either at home or in a long-term care facility. Nevertheless, despite the contraindications and risk factors, there are successful reports of NPWT in the settings of sternum osteomyelitis^[61] and exposed organs^[62].

AUTHOR RECOMMENDATIONS

At our institution, NPWT is applied for the aforementioned indications in total hip and knee arthroplasty. The quantum of negative pressure applied is typically either greater than 75 mmHg (for wound depth extending beneath fascia) or less than 75 mmHg (above fascia). Variations in pressure magnitudes for certain populations (such as pediatric and geriatric patients) are made in accordance with manufacturer guidelines and clinician judgment. Placement of NPWT must be done only after ensuring that the surrounding skin is dry enough for the adhesive material to provide an effective seal. Incisional NPWT is typically discontinued 3-5 d after surgery when there is no longer any drainage from the wound. However, NPWT dressings for deep, open wounds are changed every few days until satisfactory healing is eventually achieved. If drainage persists or is excessive in quantity, further surgical management may be necessary. In order to avoid skin maceration, the authors recommend placing the foam directly on the open wound and using protective material, such as a hydrocolloid dressing, for the surrounding skin.

PERSPECTIVES

There are currently over 60 clinical trials registered online at www.Clinicaltrials.gov, mostly concerning the prophylactic use of NPWT over high-risk closed incisions. In the adult reconstructive field, there are seven clinical trials on NPWT, all of which are evaluating its efficacy in

preventing wound complications and infections. Despite the substantial lack of evidence, the prophylactic use of single-use devices such as Prevena™ (KCI, San Antonio, Texas) and PICO™ (Smith and Nephew, Hull, United Kingdom) in patients at increased risk for postoperative drainage seems to be gaining acceptance and may potentially be incorporated in clinical guidelines for PJI prevention in the near future.

The therapeutic use of NPWT for prolonged wound drainage in an attempt to avoid the need for an I and D is still unsupported. Furthermore, Jaberi *et al.*^[63] showed that delaying surgical intervention after the onset of drainage predicts a higher failure rate once an I and D is undertaken. The role of NPWT in the management of prolonged wound drainage or acute PJI is still controversial and should not be a reason to delay surgical intervention.

CONCLUSION

The efficacy of NPWT in wound healing and its secondary benefits in terms of improving cost-effectiveness and comfort for both patient and caregiver is irrefutable. The fast expansion of indications and wide range of clinical scenarios in which it has been adopted has precluded standardization of protocols and large scale studies. For this reason, the use of NPWT still relies heavily on empirical data. Within hip and knee reconstructive surgery, the most commonly accepted use of NPWT is for the prophylaxis of wound complications in high-risk closed surgical wounds. There is a dire need for unconflicted, standardized and larger volume studies to validate this practice and to establish the role that NPWT may have in the treatment of prolonged wound drainage and acute PJI.

REFERENCES

- 1 Sheppard MD. Sealed drainage of wounds. *Lancet* 1952; **1**: 1174-1176 [PMID: 14939746 DOI: 10.1016/S0140-6736(52)91084-2]
- 2 Raffl AB. The use of negative pressure under skin flaps after radical mastectomy. *Ann Surg* 1952; **136**: 1048 [PMID: 12986694 DOI: 10.1097/0000658-195212000-00022]
- 3 Silvis RS, Potter LE, Robinson DW, Hughes WF. The use of continuous suction negative pressure instead of pressure dressing. *Ann Surg* 1955; **142**: 252-256 [PMID: 13239059 DOI: 10.1097/0000658-195508000-00011]
- 4 Braakenburg A, Obdeijn MC, Feitz R, van Rooij IA, van Griethuysen AJ, Klinkenbijn JH. The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: a randomized controlled trial. *Plast Reconstr Surg* 2006; **118**: 390-397; discussion 398-400 [PMID: 16874208 DOI: 10.1097/01.prs.0000227675.63744.af]
- 5 Perez D, Bramkamp M, Exe C, von Ruden C, Ziegler A. Modern wound care for the poor: a randomized clinical trial comparing the vacuum system with conventional saline-soaked gauze dressings. *Am J Surg* 2010; **199**: 14-20 [PMID: 19362288 DOI: 10.1016/j.amjsurg.2008.12.029]
- 6 Joseph E, Hamori C, Bergam S, Roaf E, Swann N, Anastasi G. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic nonhealing wounds. *Wounds* 2000; **12**: 60-67

- 7 **Mouës CM**, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: a prospective randomized trial. *Wound Repair Regen* 2004; **12**: 11-17 [PMID: 14974959 DOI: 10.1111/j.1067-1927.2004.12105.x]
- 8 **Wanner MB**, Schwarzl F, Strub B, Zaech GA, Pierer G. Vacuum-assisted wound closure for cheaper and more comfortable healing of pressure sores: a prospective study. *Scand J Plast Reconstr Surg Hand Surg* 2003; **37**: 28-33 [PMID: 12625392 DOI: 10.1080/713796078]
- 9 **Eginton MT**, Brown KR, Seabrook GR, Towne JB, Cambria RA. A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds. *Ann Vasc Surg* 2003; **17**: 645-649 [PMID: 14534844 DOI: 10.1007/s10016-003-0065-3]
- 10 **Armstrong DG**, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet* 2005; **366**: 1704-1710 [PMID: 16291063 DOI: 10.1016/S0140-6736(05)67695-7]
- 11 **Ford CN**, Reinhard ER, Yeh D, Syrek D, De Las Morenas A, Bergman SB, Williams S, Hamori CA. Interim analysis of a prospective, randomized trial of vacuum-assisted closure versus the healthpoint system in the management of pressure ulcers. *Ann Plast Surg* 2002; **49**: 55-61; discussion 61 [PMID: 12142596 DOI: 10.1097/0000637-200207000-00009]
- 12 **Moisidis E**, Heath T, Boorer C, Ho K, Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg* 2004; **114**: 917-922 [PMID: 15468399 DOI: 10.1097/01.PRS.0000133168.57199.E1]
- 13 **Plikaitis CM**, Molnar JA. Subatmospheric pressure wound therapy and the vacuum-assisted closure device: basic science and current clinical successes. *Expert Rev Med Devices* 2006; **3**: 175-184 [PMID: 16515384 DOI: 10.1586/17434440.3.2.175]
- 14 **Morykwas MJ**, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg* 1997; **38**: 553-562 [PMID: 9188970 DOI: 10.1097/0000637-199706000-00001]
- 15 **Ubbink DT**, Westerbos SJ, Nelson EA, Vermeulen H. A systematic review of topical negative pressure therapy for acute and chronic wounds. *Br J Surg* 2008; **95**: 685-692 [PMID: 18446777 DOI: 10.1002/bjs.6238]
- 16 **Patel VP**, Walsh M, Sehgal B, Preston C, DeWal H, Di Cesare PE. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *J Bone Joint Surg Am* 2007; **89**: 33-38 [PMID: 17200307 DOI: 10.2106/JBJS.F.00163]
- 17 **Saleh K**, Olson M, Resig S, Bershadsky B, Kuskowski M, Gioe T, Robinson H, Schmidt R, McElfresh E. Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res* 2002; **20**: 506-515 [PMID: 12038624 DOI: 10.1016/S0736-0266(01)00153-X]
- 18 **Fox JW**, Golden GT. The use of drains in subcutaneous surgical procedures. *Am J Surg* 1976; **132**: 673-674 [PMID: 984318 DOI: 10.1016/0002-9610(76)90372-X]
- 19 **Argenta LC**, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. *Ann Plast Surg* 1997; **38**: 563-576; discussion 577 [PMID: 9188971 DOI: 10.1097/0000637-199706000-00002]
- 20 **Fleischmann W**, Strecker W, Bombelli M, Kinzl L. [Vacuum sealing as treatment of soft tissue damage in open fractures]. *Unfallchirurg* 1993; **96**: 488-492 [PMID: 8235687]
- 21 **Fleischmann W**, Lang E, Kinzl L. [Vacuum assisted wound closure after dermatofasciotomy of the lower extremity]. *Unfallchirurg* 1996; **99**: 283-287 [PMID: 8658208]
- 22 **Greer SE**, Longaker MT, Margiotta M, Mathews AJ, Kasabian A. The use of subatmospheric pressure dressing for the coverage of radial forearm free flap donor-site exposed tendon complications. *Ann Plast Surg* 1999; **43**: 551-554 [PMID: 10560875 DOI: 10.1097/0000637-199911000-00016]
- 23 **Wolvos T**. Wound instillation--the next step in negative pressure wound therapy. Lessons learned from initial experiences. *Ostomy Wound Manage* 2004; **50**: 56-66 [PMID: 15545698]
- 24 **Shweiki E**, Gallagher KE. Negative pressure wound therapy in acute, contaminated wounds: documenting its safety and efficacy to support current global practice. *Int Wound J* 2013; **10**: 13-43 [PMID: 22420782 DOI: 10.1111/j.1742-481X.2012.00940.x]
- 25 **Taylor DF**, Smith FB. Porous methyl methacrylate as an implant material. *J Biomed Mater Res* 1972; **6**: 467-479 [PMID: 5014905 DOI: 10.1002/jbm.820060112]
- 26 **Wake MC**, Patrick CW, Mikos AG. Pore morphology effects on the fibrovascular tissue growth in porous polymer substrates. *Cell Transplant* 1994; **3**: 339-343 [PMID: 7522866]
- 27 **Morykwas MJ**, Falser BJ, Pearce DJ, Argenta LC. Effects of varying levels of subatmospheric pressure on the rate of granulation tissue formation in experimental wounds in swine. *Ann Plast Surg* 2001; **47**: 547-551 [PMID: 11716268 DOI: 10.1097/0000637-200111000-00013]
- 28 **Haghshenasskashani A**, Varcoe RI. A new negative pressure dressing (Prevena) to prevent wound complications following lower limb disal arterial bypass. *Br J Diabetes Vasc Dis* 2011; **11**: 21-24
- 29 **Bollero D**, Degano K, Gangemi EN, Aloj D, Malvasio V, Stella M. Long-term follow-up of negative pressure wound therapy with instillation: a limb salvage procedure? *Int Wound J* 2014 Sep 19; Epub ahead of print [PMID: 25234266 DOI: 10.1111/iwj.12373]
- 30 **Wolvos TA**. Negative pressure wound therapy with instillation: the current state of the art. *Surg Technol Int* 2014; **24**: 53-62 [PMID: 24574014]
- 31 **Payne JL**, Ambrosio AM. Evaluation of an antimicrobial silver foam dressing for use with V.A.C. therapy: morphological, mechanical, and antimicrobial properties. *J Biomed Mater Res B Appl Biomater* 2009; **89**: 217-222 [PMID: 19274724 DOI: 10.1002/jbm.b.31209]
- 32 **Sachsenmaier S**, Peschel A, Ipach I, Kluba T. Antibacterial potency of V.A.C. GranuFoam Silver(®) Dressing. *Injury* 2013; **44**: 1363-1367 [PMID: 23928285 DOI: 10.1016/j.injury.2013.07.014]
- 33 **Huang C**, Leavitt T, Bayer LR, Orgill DP. Effect of negative pressure wound therapy on wound healing. *Curr Probl Surg* 2014; **51**: 301-331 [PMID: 24935079 DOI: 10.1067/j.cpsurg.2014.04.001]
- 34 **Glass GE**, Murphy GF, Esmaeili A, Lai LM, Nanchahal J. Systematic review of molecular mechanism of action of negative-pressure wound therapy. *Br J Surg* 2014; **101**: 1627-1636 [PMID: 25294112 DOI: 10.1002/bjs.9636]
- 35 **Erba P**, Ogawa R, Ackermann M, Adini A, Miele LF, Dastouri P, Helm D, Mentzer SJ, D'Amato RJ, Murphy GF, Konerding MA, Orgill DP. Angiogenesis in wounds treated by microdeformational wound therapy. *Ann Surg* 2011; **253**: 402-409 [PMID: 21217515 DOI: 10.1097/SLA.0b013e31820563a8]
- 36 **McNulty AK**, Schmidt M, Feeley T, Kieswetter K. Effects of negative pressure wound therapy on fibroblast viability, chemotactic signaling, and proliferation in a provisional wound (fibrin) matrix. *Wound Repair Regen* 2007; **15**: 838-846 [PMID: 18028132 DOI: 10.1111/j.1524-475X.2007.00287.x]
- 37 **Lu F**, Ogawa R, Nguyen DT, Chen B, Guo D, Helm DL, Zhan Q, Murphy GF, Orgill DP. Microdeformation of three-dimensional cultured fibroblasts induces gene expression and morphological changes. *Ann Plast Surg* 2011; **66**: 296-300 [PMID: 21233699 DOI: 10.1097/SAP.0b013e3181ea1e9b]
- 38 **Younan G**, Ogawa R, Ramirez M, Helm D, Dastouri P, Orgill DP. Analysis of nerve and neuropeptide patterns in vacuum-assisted closure-treated diabetic murine wounds. *Plast Reconstr Surg* 2010; **126**: 87-96 [PMID: 20595860 DOI: 10.1097/PRS.0b013e3181da86d0]
- 39 **Torbrand C**, Wackenfors A, Lindstedt S, Ekman R, Ingemansson R, Malmjö M. Sympathetic and sensory nerve activation during negative pressure therapy of sternotomy wounds. *Interact Cardiovasc Thorac Surg* 2008; **7**: 1067-1070 [PMID: 18784122 DOI: 10.1510/icvts.2008.181792]
- 40 **Scherer SS**, Pietramaggiori G, Mathews JC, Prsa MJ, Huang S, Orgill DP. The mechanism of action of the vacuum-assisted closure device. *Plast Reconstr Surg* 2008; **122**: 786-797 [PMID: 18766042]

- DOI: 10.1097/PRS.0b013e31818237ac]
- 41 **Saxena V**, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. *Plast Reconstr Surg* 2004; **114**: 1086-1096; discussion 1097-1098 [PMID: 15457017 DOI: 10.1097/01.PRS.0000135330.51408.97]
 - 42 **Ingber DE**. The mechanochemical basis of cell and tissue regulation. *Mech Chem Biosyst* 2004; **1**: 53-68 [PMID: 16783946]
 - 43 **Adámková M**, Tymonová J, Zámečnicková I, Kadlcík M, Klosová H. First experience with the use of vacuum assisted closure in the treatment of skin defects at the burn center. *Acta Chir Plast* 2005; **47**: 24-27 [PMID: 15954460]
 - 44 **Lancerotto L**, Bayer LR, Orgill DP. Mechanisms of action of microdeformational wound therapy. *Semin Cell Dev Biol* 2012; **23**: 987-992 [PMID: 23036531 DOI: 10.1016/j.semdb.2012.09.009]
 - 45 **Labanaris AP**, Polykandriotis E, Horch RE. The effect of vacuum-assisted closure on lymph vessels in chronic wounds. *J Plast Reconstr Aesthet Surg* 2009; **62**: 1068-1075 [PMID: 18524708 DOI: 10.1016/j.bjps.2008.01.006]
 - 46 **Winter GD**, Scales JT. Effect of air drying and dressings on the surface of a wound. *Nature* 1963; **197**: 91-92 [PMID: 14001241 DOI: 10.1038/197091b0]
 - 47 **Orgill DP**, Manders EK, Sumpio BE, Lee RC, Attinger CE, Gurtner GC, Ehrlich HP. The mechanisms of action of vacuum assisted closure: more to learn. *Surgery* 2009; **146**: 40-51 [PMID: 19541009 DOI: 10.1016/j.surg.2009.02.002]
 - 48 **Gerry R**, Kwei S, Bayer L, Breuing KH. Silver-impregnated vacuum-assisted closure in the treatment of recalcitrant venous stasis ulcers. *Ann Plast Surg* 2007; **59**: 58-62 [PMID: 17589262 DOI: 10.1097/01.sap.0000263420.70303.cc]
 - 49 **Karlakki S**, Brem M, Giannini S, Khanduja V, Stannard J, Martin R. Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery: A review of evidence and mechanisms for an emerging indication. *Bone Joint Res* 2013; **2**: 276-284 [PMID: 24352756 DOI: 10.1302/2046-3758.212.2000190]
 - 50 **Gomoll AH**, Lin A, Harris MB. Incisional vacuum-assisted closure therapy. *J Orthop Trauma* 2006; **20**: 705-709 [PMID: 17106382 DOI: 10.1097/01.bot.0000211159.98239.d2]
 - 51 **Kirr R**, Wiberg J, Hertlein H. [Clinical experience and results of using the V.A.C. instill therapy in infected hip- and knee prosthetics]. *Zentralbl Chir* 2006; **131** Suppl 1: S79-S82 [PMID: 16575651 DOI: 10.1055/s-2005-921501]
 - 52 **Lehner B**, Bernd L. [V.A.C.-instill therapy in periprosthetic infection of hip and knee arthroplasty]. *Zentralbl Chir* 2006; **131** Suppl 1: S160-S164 [PMID: 16575671 DOI: 10.1055/s-2006-921513]
 - 53 **Kelm J**, Schmitt E, Anagnostakos K. Vacuum-assisted closure in the treatment of early hip joint infections. *Int J Med Sci* 2009; **6**: 241-246 [PMID: 19834589 DOI: 10.7150/ijms.6.241]
 - 54 **Howell RD**, Hadley S, Strauss E, Pelham FR. Blister formation with negative pressure dressings after total knee arthroplasty. *Curr Orthop Pract* 2011; **22**: 176-179 [DOI: 10.1097/BCO.0b013e31820b3e21]
 - 55 **Pachowsky M**, Gusinde J, Klein A, Lehl S, Schulz-Drost S, Schlechtweg P, Pauser J, Gelse K, Brem MH. Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty. *Int Orthop* 2012; **36**: 719-722 [PMID: 21761149 DOI: 10.1007/s00264-011-1321-8]
 - 56 **Hansen E**, Durinka JB, Costanzo JA, Austin MS, Deirmengian GK. Negative pressure wound therapy is associated with resolution of incisional drainage in most wounds after hip arthroplasty. *Clin Orthop Relat Res* 2013; **471**: 3230-3236 [PMID: 23539123 DOI: 10.1007/s11999-013-2937-3]
 - 57 **Pauser J**, Nordmeyer M, Biber R, Jantsch J, Kopschina C, Bail HJ, Brem MH. Incisional negative pressure wound therapy after hemiarthroplasty for femoral neck fractures - reduction of wound complications. *Int Wound J* 2014 Aug 14; Epub ahead of print [PMID: 25125244 DOI: 10.1111/iwj.12344]
 - 58 **Agency for Healthcare Research and Quality, United States Department of Health and Human Services**. Technology assessment: negative pressure wound therapy devices [WWW document]. Available from: URL: <http://www.ahrq.gov/clinic/ta/negpresswtd/npwt02.htm>
 - 59 **Argenta LC**, Morykwas MJ, Marks MW, DeFranzo AJ, Molnar JA, David LR. Vacuum-assisted closure: state of clinic art. *Plast Reconstr Surg* 2006; **117**: 127S-142S [PMID: 16799380 DOI: 10.1097/01.prs.0000222551.10793.51]
 - 60 **Gwan-Nulla DN**, Casal RS. Toxic shock syndrome associated with the use of the vacuum-assisted closure device. *Ann Plast Surg* 2001; **47**: 552-554 [PMID: 11716269 DOI: 10.1097/00000637-200111000-00014]
 - 61 **Tocco MP**, Ballardini M, Masala M, Perozzi A. Post-sternotomy chronic osteomyelitis: is sternal resection always necessary? *Eur J Cardiothorac Surg* 2013; **43**: 715-721 [PMID: 22869252 DOI: 10.1093/ejcts/ezs449]
 - 62 **Sermoneta D**, Di Mugno M, Spada PL, Lodoli C, Carvelli ME, Magalini SC, Cavicchioni C, Bocci MG, Martorelli F, Brizi MG, Gui D. Intra-abdominal vacuum-assisted closure (VAC) after necrosectomy for acute necrotising pancreatitis: preliminary experience. *Int Wound J* 2010; **7**: 525-530 [PMID: 20726923 DOI: 10.1111/j.1742-481X.2010.00727.x]
 - 63 **Jaberi FM**, Parvizi J, Haytmanek CT, Joshi A, Purtill J. Procrastination of wound drainage and malnutrition affect the outcome of joint arthroplasty. *Clin Orthop Relat Res* 2008; **466**: 1368-1371 [PMID: 18404297 DOI: 10.1007/s11999-008-0214-7]

P- Reviewer: Patra SR, Tangtrakulwanich B

S- Editor: Gong XM **L- Editor:** A **E- Editor:** Li D



Direct anterior total hip arthroplasty: Literature review of variations in surgical technique

Keith P Connolly, Atul F Kamath

Keith P Connolly, Atul F Kamath, Department of Orthopedic Surgery, Center for Hip Preservation, Pennsylvania Hospital, University of Pennsylvania, Philadelphia, PA 19107, United States

Author contributions: Connolly KP and Kamath AF equally contributed to this paper.

Conflict-of-interest statement: The authors have no conflicts of interest to disclose pertaining to the subject of this review manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Atul F Kamath, MD, Department of Orthopedic Surgery, Center for Hip Preservation, Pennsylvania Hospital, University of Pennsylvania, 800 Spruce Street, 8th Floor Preston, Philadelphia, PA 19107, United States. akamath@post.harvard.edu
 Telephone: +1-215-6878169
 Fax: +1-215-8292492

Received: May 27, 2015

Peer-review started: May 30, 2015

First decision: August 4, 2015

Revised: October 11, 2015

Accepted: November 3, 2015

Article in press: November 4, 2015

Published online: January 18, 2016

Abstract

The direct anterior approach to the hip has been suggested to have several advantages compared to previously popular approaches through its use of an intra-muscular and intra-nervous interval between

the tensor fasciae latae and sartorius muscles. Recent increased interest in tissue-sparing and minimally-invasive arthroplasty has given rise to a sharp increase in the utilization of direct anterior total hip arthroplasty. A number of variations of the procedure have been described and several authors have published their experiences and feedback to successfully accomplishing this procedure. Additionally, improved understanding of relevant soft tissue constraints and anatomic variants has provided improved margin of safety for patients. The procedure may be performed using specially-designed instruments and a fracture table, however many authors have also described equally efficacious performance using a regular table and standard arthroplasty tools. The capacity to utilize fluoroscopy intra-operatively for component positioning is a valuable asset to the approach and can be of particular benefit for surgeons gaining familiarity. Proper management of patient and limb positioning are vital to reducing risk of intra-operative complications. An understanding of its limitations and challenges are also critical to safe employment. This review summarizes the key features of the direct anterior approach for total hip arthroplasty as an aid to improving the understanding of this important and effective method for modern hip replacement surgeons.

Key words: Anterior hip arthroplasty; Anterior supine intramuscular approach; Total hip arthroplasty; Direct anterior approach

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This review captures the most important concepts of direct anterior total hip arthroplasty as described by numerous surgeons' experiences with the procedure. It compares variations in surgical exposure and arthroplasty techniques, while identifying key elements of the anterior hip anatomy for performance of safe and efficient surgery. The review divides anterior hip arthroplasty into six distinct elements, citing the

most relevant pearls and pitfalls of previous publications and the most relied upon surgical methods. This concise summary can be beneficial to any level of surgeon desiring to enhance their understanding of direct anterior total hip arthroplasty.

Connolly KP, Kamath AF. Direct anterior total hip arthroplasty: Literature review of variations in surgical technique. *World J Orthop* 2016; 7(1): 38-43 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/38.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.38>

INTRODUCTION

The direct anterior approach (DAA) to the hip was first described by Carl Hueter in 1881. However Marius Smith-Petersen is frequently credited with developing this technique due to his prolific use of the technique throughout his career, after initially publishing his description in 1917. Modern day literature frequently refers to this method interchangeably as both the Hueter and Smith-Petersen approach when identifying the anterior based incision that utilizes the interval to the hip joint through the tensor fasciae latae (TFL) and the sartorius muscles^[1]. Light and Keggi^[2] published their extensive experience using this approach for hip arthroplasty in 1980, and the Judets described the procedure with use of a fracture table in 1985^[1,2]. The modern day desire to perform hip reconstruction through less invasive and tissue sparing methods was the key driver in the newfound interest of the anterior approach. This has led to a surge in its proliferation over the past 15 years^[3]. During this time, numerous authors have described variations of the technique and key concepts to safe and successful performance of hip arthroplasty. Although many consider the DAA appropriate exclusively for primary joint replacement, several authors have noted routine use of this technique for complex revision surgery and bipolar hemiarthroplasty for hip fractures^[4-6]. This review seeks to summarize the published literature on the direct anterior total hip arthroplasty procedure with a focus on comparative key pearls and pitfalls.

INDICATIONS AND CHALLENGES

Several authors have recommended using the DAA in patients of nearly all body habitus and hip conditions^[4,7]. The ideal patient has been described as a flexible, non-muscular patient with valgus femoral neck and good femoral offset. It is reasonable to initially develop skills to perform the approach in slender patients with a body mass index of less than thirty^[8]. As achievement of appropriate exposure is gained with experience using the technique, it has also been suggested that lack of appropriate instrumentation designed for anterior supine intramuscular approach is a contraindication^[8]. Some anatomic features of the native hip and pelvis

are recognized to make the DAA more difficult. A wide or horizontal iliac wing limits access to the femoral canal for broaching and femoral component placement. Acetabular protrusion brings the femoral canal closer to pelvis and obstructs access to femur. A neck shaft angle with decreased offset positions the femoral canal deeper in the thigh, and anatomy associated with obese muscular males limits the space available to place components^[9]. One disadvantage of the anterior approach is diminished access to the posterior column. If the patient has a deficient posterior acetabular wall from previous hardware or trauma, or if posterior acetabular augmentation is contemplated, the anterior exposure may be unsuitable^[10].

SURGICAL TECHNIQUE

Patient positioning

The vast majority of authors describing the DAA position the patient supine on a fracture or regular table. Michel *et al*^[11] also proposed performing anterior total hip arthroplasty (THA) using lateral decubitus positioning. When using a regular table, the patient is positioned with the pelvis located over the table break, which can be angled to allow hyperextension at the hip joint (Figure 1A). A bump may be used placed under the sacrum, centered at the anterior superior iliac spine (ASIS) to further elevate the pelvis^[3]. Kennon *et al*^[12] recommends orienting the table at right angles to the walls for accurate referencing and anatomic orientation. The contralateral leg is frequently draped into the field, and an arm board may be placed alongside to allow for abduction during femoral exposure^[8]. Obese patients should have the pannus retracted with adhesive tape to avoid interference with exposure^[7]. With use a fracture table (Figure 1B), the peroneal post should be well-padded to avoid peroneal nerve neuropraxia^[13].

Surgical approach

The descriptions for skin incision vary by surgeon, however most authors rely on the ASIS and greater trochanter as anatomic landmarks for reference (Figure 2). An oblique incision is made originating 2-4 cm distal and lateral to the ASIS to a point a few finger breaths anterior to the greater trochanter^[4,7,8,11,14,15]. A cadaveric anatomy study showed that the zone immediately distal to the intertrochanteric line formed an anatomic barrier to protect neurovascular structures. Incision extension distal to this point risks damage to branches of the lateral femoral circumflex artery (LFCA) supplying the proximal quadriceps muscles and femoral nerve divisions to the vastus intermedius and lateralis^[16]. The incision is generally oriented in line with the TFL, which can also be delineated by a line from the ASIS to the patella or fibular head, or in line with the femoral neck^[17]. Fluoroscopy may be used to assist in identifying the femoral neck and midpoint for the incision^[18].

A well-recognized complication of this approach is the proximity of the incision to the lateral femoral

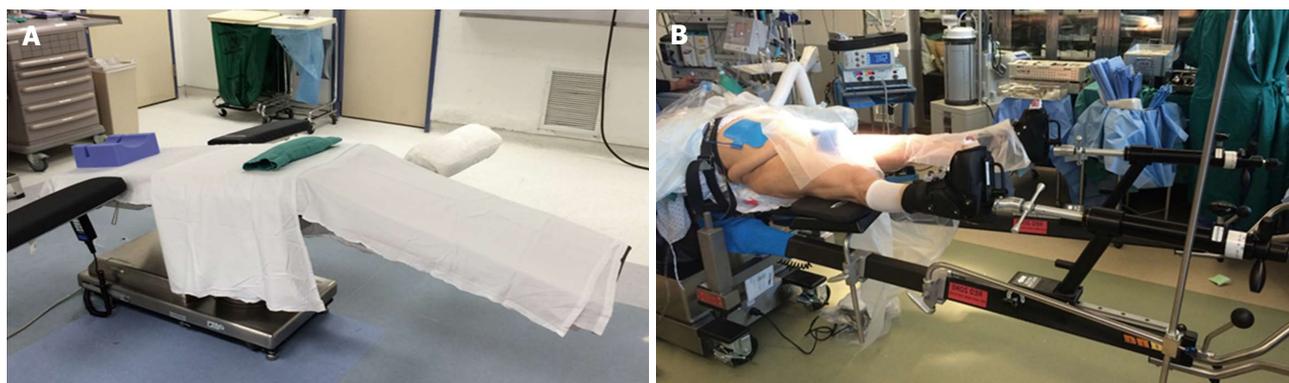


Figure 1 Patient positioning. A: Use of a regular table with bump under the sacrum and ability to lower the distal end of the bed down to afford better femoral exposure. An extra arm board can be placed on the contralateral distal end of the bed to support the contralateral leg while accessing the operative femoral canal; B: Patient positioning on a fracture-type table (Hana table, Mizuho Orthopedics Systems, Inc.).

cutaneous nerve (LFCN). Though it is commonly believed that remaining lateral to the TFL/sartorius interval reduces risk for injury to the nerve, a cadaveric study of LFCN arborization showed the gluteal branch crossed the anterior margin of the TFL at 44 mm from the ASIS; the femoral branch also crossed this margin in half of specimens, at an average of 46 mm distal to the ASIS^[19,20]. A 10% variation in branches was found in a study of 60 cadavers^[21]. De Geest *et al*^[22] found a decreased incidence of LFCN injury by further lateralizing their incision. Blunt dissection through the subcutaneous fat is recommended to further minimize risk of nerve injury^[7]. Damage to the medial subcutaneous fat pad should be avoided to prevent injury to the trunk of the LFCN, which can result in meralgia paresthetica^[8].

The interval between the TFL and sartorius is entered by incising the fascia over the medial TFL muscle belly, retaining an adequate sleeve of tissue for closure and offering protection to the LFCN^[4,15,23]. Care should be taken to ensure the appropriate interval, as dissection through the lateral TFL and not in the intramuscular portal may result in damage to the motor branch of the superior gluteal nerve^[7]. If the exposure is too posterior, blood vessels will be seen entering the fascia and the fascia becomes denser as it overlies the gluteus medius, which should prompt recognition of the improper interval^[15]. Conversely, if the plane is developed too medially, dissection in to the femoral triangle will occur, risking injury to the femoral neurovascular bundle^[19]. Blunt dissection separates the TFL muscle belly from the fascia and facilitates entry into the interval for proper exposure of the hip capsule.

Hip exposure

A sharp retractor may be placed around the greater trochanter and the rectus femoris can be retracted medially with a rake or Hibbs retractor^[8]. The ascending branches of the LFCN usually lie in the distal portion of the approach, though can be somewhat variable in location and extent; these vessels should now be visualized and ligated with electrocautery or hand suture tie. Some surgeons have employed bipolar sealing technology

for the purposes of vessel coagulation and hemostasis throughout the procedure. The instrumentation is replaced with a curved retractor over the superior capsule to retract the TFL superiorly. A second cobra or Hohmann can be placed in a "soft spot" proximal to the vastus lateralis, on the medial of the neck to retract the rectus femoris and sartorius medially. Overzealous retraction should be avoided to minimize damage to the TFL and rectus, as well as to avoid neurovascular traction.

Specialized retractors with extra-depth blades and curved sides (Figure 3) are also available for minimally invasive surgery to facilitate gentle soft tissue handling^[19]. In muscular patients, the rectus femoris and TFL insertions near the ASIS may be elevated to facilitate exposure^[7]. A capsulotomy or capsulectomy of the anterior capsule have both been described. Some authors advocate removal of the capsule to facilitate exposure. However, retaining a medial portion may provide a sleeve of tissue between the iliopsoas tendon and acetabular rim to reduce irritation^[13,24,25]. Kennon *et al*^[12] advised removal of a thick, contracted anterior capsule to prevent impingement possibly contributing to posterior dislocation. Positioning the operative leg in a figure-four position on a regular table can assist in release of the anterolateral and inferior capsule in the calcar region^[15,23]. Release of the superior capsule has been shown in a cadaveric study to be the most crucial in allowing elevation of the femur, which was not increased with release of the posterior capsule^[26]. Following capsular release, attention is then turned to the femoral neck and head.

The visible labrum and anterior osteophytes may be excised to assist in removal of the femoral head, but this is often not necessary. Medial and lateral retractors are repositioned within the capsule around the femoral neck. The head may be removed by performing a femoral neck cut and placing a corkscrew in the head, or by first excising a "napkin ring" section of the neck. Placement of a hip skid along the anterior acetabulum with a slightly distracted femoral head, *via* traction to the limb or instrumentation in the head, can facilitate head removal and transection of the ligamentum teres^[13,27]. Gentle

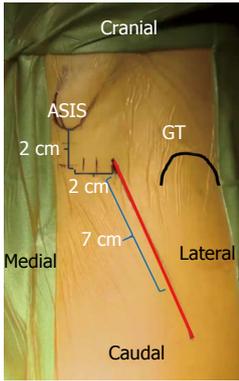


Figure 2 Surface anatomy for the direct anterior approach. A 6-8 cm oblique incision is typically used by the authors. This incision may be extended proximally and distally as needed along the Smith-Petersen interval for adequate femoral and acetabular exposure.

external rotation can help with dislocation. If not already done so, the femoral neck cut based on pre-operative planning is performed, with completion of the cut near the greater trochanter finished using an osteotome to reduce the risk of fracture by an oscillating saw.

Acetabulum

A sharp retractor may be inserted at the ventral acetabular rim, keeping the retractor immediately adjacent to the bone to avoid femoral nerve compression^[19]. Some surgeons use a light-mounted retractor in this position to improve visualization. Additional retractors are frequently placed at the posterior acetabulum and at the level of the transverse acetabular ligament. Remaining labrum and obstructing osteophytes are removed from the acetabulum, and reaming is commenced. Most surgeons performing this approach advocate use of specialized offset instruments. However, a straight reamer can be used with adequate exposure and careful attention to avoid leverage of the anterior acetabulum to prevent eccentric anterior reaming. Post *et al*^[3] also recommend positioning the reamer head first and then attaching the handle for challenging access. If performing the procedure in the lateral decubitus position, visualization of the anterior acetabulum is difficult and can complicate reaming and cup placement.

Assessing the native pelvis to assist proper cup positioning may be accomplished by palpating the anterior superior iliac spines^[19]. Although there is a tendency towards over-anteverting the cup with this approach by holding the cup positioner too vertical, an advantage of the supine DAA is the ability to utilize fluoroscopy intra-operatively^[19]. Many surgeons recommend reaming and cup placement using image guidance, particularly in initial adoption of the technique. A press-fit acetabular cup may be inserted with a target abduction angle of 35-45 degrees and anteversion of 10-20 degrees.

Of note, a study of fluoroscopy-guided anterior hip arthroplasty found an early higher rate of dislocation using a goal of 10-30 degrees of anteversion, which was improved by adjusting the target angle to 5-25



Figure 3 Selected retractors used for direct anterior approach. From left to right, hip skid for ceramic head reduction, greater trochanteric retractor/elevator, femoral elevator for medial/calcar exposure (front and side views), medial acetabular wall retractor, posterior acetabular wall retractor, and tensor fascia lata retractor.

degrees^[28]. Computer aided navigation has also been described to improve accuracy of cup placement. A study of computed tomography-based hip navigation comparing mini-anterior and mini-posterior found an accuracy of 2.0 degrees for abduction and 2.7 degrees for anteversion of cup placement with the anterior approach. Surface registration took one minute longer in the anterior approach but operative time was not significantly different^[29]. A review of 300 DAA hips, half performed with computer aided navigation, showed decreased operative times with navigation and greater accuracy of abduction angles^[30]. Following placement of the cup, an acetabular liner is inserted and acetabular retractors are removed.

Femur

The femur may be exposed on a fracture table by dropping the limb spar to the floor, with all traction removed, by a non-scrubbed assistant, along with external rotation and adduction of the limb. Adequate soft tissue capsular releases about the proximal femur should be performed prior to this maneuver. Matta *et al*^[27] utilized a scrubbed assistant to provide additional external rotation force at the femoral condyles using to reduce the stresses generated by the traction boots across the ankle, which can subject patients to iatrogenic ankle fracture. A retractor should be located at the calcar region, and a second retractor at the lateral greater trochanter during this maneuver. Release of the posterosuperior capsule will aid in clearance of the greater trochanter from behind the acetabular rim^[8].

Using a regular table, this exposure is performed by dropping the distal end of the table and by placing the bed in a Trendelenburg position, forming an inverted V-shape of the body for hyperextension at the hip. Trendelenburg positioning may alternatively be established at the onset of the case; however, patients undergoing general anesthesia may be at higher risk for gastrointestinal reflux^[13]. The contralateral leg may be placed on a mounted arm board or padded Mayo stand

to allow for adduction of the operative limb under the contralateral leg in a figure-of-four position on a regular table^[24]. For lateral decubitus positioning, the operative limb is abducted, hyperextended, externally rotated and flexed at the knee, with the foot positioned into a sterile bag posterior to the patient.

Elevation of the femur may be accomplished using a hydraulic lift hook or manual placement of a hook just distal to the vastus ridge around the posterior femur. Tension on the femur can be appreciated through tactile and visual feedback of the retractor behind the greater trochanter. In cases where the femur is unable to be appreciably exposed using these maneuvers, Moskal *et al*^[9] described sequential releases of soft tissue along the medial greater trochanter and femoral neck under tension, progressing through the release of hip capsule, piriformis, gemelli, and obturator internus. Posterior circumflex vessels should be identified and cauterized with these releases^[12]. The obturator externus provides hip stability through the most medial pull of the femur to the pelvis and should not be released unless necessary^[9]. Adequate entry to the femur should be verified with removal of interfering bone or tissue by rongeur or box cutter to prevent varus stem positioning^[13]. A high-speed burr may also be used as necessary.

Offset hand instruments may be preferred for broaching and stem placement. An alternative method to providing access utilizes a separate stab wound proximally in line with the femoral canal. This technique may be useful in large or muscular patients and for revision arthroplasty, and can prevent the need for extensive posterior releases^[12]. As femoral perforations are a known early complication of this approach, Post *et al*^[3] recommended identifying the trajectory of the canal through use of a guide wire on a T-handle. The femur is then broached and the trial component inserted. Reduction of the hip is performed by reversal of the steps utilized in exposing the femur. Fluoroscopy can be used to assess the adequacy of components, and a stability assessment is performed, emphasizing careful attention to extremes of external rotation and extension. Leg lengths may be compared directly on a regular table or by utilizing radiographic comparison to the contralateral limb with a fracture table^[13-15]. Final components are then placed in a similar fashion, and a final stability examination is performed.

Closure

The wound is thoroughly irrigated, and closure is performed according to surgeon preference. If capsulotomy was made, the flaps may be approximated. Hematoma prevention requires adequate hemostasis, as there is higher predilection for hematoma formation with less inherent gravity pressure over an anterior wound compared to other approaches. Furthermore, the risk for hematoma to track deeply exists as the only layer routinely closed is the tensor sheath^[31]. Suturing of the tensor fascia latae should be performed with care to avoid damage to the LFCN medially. The subcutaneous

tissue and skin are closed in a standard fashion. Many surgeons choose to leave a drain in place beneath the fascial layer; however, a study of 120 patients comparing drain utilization found that patients without drains had an earlier dry surgical site and were discharged from the hospital on average one day earlier. There was a non-significant trend toward high pain scores on post-operative day one, with increased thigh swelling on post-operative day two. There were no difference in transfusion requirements between the groups^[32].

CONCLUSION

All approaches to the hip have been shown to be safe and effective with proper training and meticulous technique. The DAA to the hip has gained significant popularity recently, and can be a valuable tool for hip replacement in most patients. This review examines the published variations of direct anterior THA, showing that several facets of the procedure can be tailored to a given surgeon's preference or the particular needs of the patient anatomy. Familiarity with the surgical anatomy and understanding the limitations of the anterior hip approach are key to successful execution. The growing desire for less invasive arthroplasty with improvement in functional results makes this approach an attractive choice for surgeons.

REFERENCES

- 1 **Rachbauer F**, Kain MS, Leunig M. The history of the anterior approach to the hip. *Orthop Clin North Am* 2009; **40**: 311-320 [PMID: 19576398 DOI: 10.1016/j.ocl.2009.02.007]
- 2 **Light TR**, Keggi KJ. Anterior approach to hip arthroplasty. *Clin Orthop Relat Res* 1980; (**152**): 255-260 [PMID: 7438611 DOI: 10.1097/00003086-198010000-00029]
- 3 **Post ZD**, Orozco F, Diaz-Ledezma C, Hozack WJ, Ong A. Direct Anterior Approach for Total Hip Arthroplasty: Indications, Technique, and Results. *J Am Acad Orthop Surg* 2014; **22**: 595-603 [PMID: 25157041 DOI: 10.5435/JAAOS-22-09-595]
- 4 **Kennon R**, Keggi J, Zatorski LE, Keggi KJ. Anterior approach for total hip arthroplasty: beyond the minimally invasive technique. *J Bone Joint Surg Am* 2004; **86-A** Suppl 2: 91-97 [PMID: 15691113]
- 5 **Mast NH**, Laude F. Revision total hip arthroplasty performed through the Hueter interval. *J Bone Joint Surg Am* 2011; **93** Suppl 2: 143-148 [PMID: 21543704 DOI: 10.2106/JBJS.J.01736]
- 6 **Unger AC**, Schulz AP, Paech A, Jürgens Ch, Renken FG. Modified direct anterior approach in minimally invasive hip hemiarthroplasty in a geriatric population: a feasibility study and description of the technique. *Arch Orthop Trauma Surg* 2013; **133**: 1509-1516 [PMID: 23979693 DOI: 10.1007/s00402-013-1831-5]
- 7 **Bal BS**, Vallurupalli S. Minimally invasive total hip arthroplasty with the anterior approach. *Indian J Orthop* 2008; **42**: 301-308 [PMID: 19753156 DOI: 10.4103/0019-5413.41853]
- 8 **Bender B**, Nogler M, Hozack WJ. Direct anterior approach for total hip arthroplasty. *Orthop Clin North Am* 2009; **40**: 321-328 [PMID: 19576399 DOI: 10.1016/j.ocl.2009.01.003]
- 9 **Moskal JT**, Capps SG, Scaneli JA. Anterior muscle sparing approach for total hip arthroplasty. *World J Orthop* 2013; **4**: 12-18 [PMID: 23362470 DOI: 10.5312/wjo.v4.i1.12]
- 10 **Barrett WP**, Turner SE, Leopold JP. Prospective randomized study of direct anterior vs postero-lateral approach for total hip arthroplasty. *J Arthroplasty* 2013; **28**: 1634-1638 [PMID:

- 23523485 DOI: 10.1016/j.arth.2013.01.034]
- 11 **Michel MC**, Witschger P. MicroHip: a minimally invasive procedure for total hip replacement surgery using a modified Smith-Peterson approach. *Ortop Traumatol Rehabil* 2007; **9**: 46-51 [PMID: 17514174]
 - 12 **Kennon RE**, Keggi JM, Wetmore RS, Zatorski LE, Huo MH, Keggi KJ. Total hip arthroplasty through a minimally invasive anterior surgical approach. *J Bone Joint Surg Am* 2003; **85-A** Suppl 4: 39-48 [PMID: 14652392]
 - 13 **Horne PH**, Olson SA. Direct anterior approach for total hip arthroplasty using the fracture table. *Curr Rev Musculoskelet Med* 2011; **4**: 139-145 [PMID: 21713379 DOI: 10.1007/s12178-011-9087-6]
 - 14 **Alexandrov T**, Ahlmann ER, Menendez LR. Early clinical and radiographic results of minimally invasive anterior approach hip arthroplasty. *Adv Orthop* 2014; **2014**: 954208 [PMID: 24715984 DOI: 10.1155/2014/954208]
 - 15 **Lovell TP**. Single-incision direct anterior approach for total hip arthroplasty using a standard operating table. *J Arthroplasty* 2008; **23**: 64-68 [PMID: 18922376 DOI: 10.1016/j.arth.2008.06.027]
 - 16 **Grob K**, Monahan R, Gilbey H, Yap F, Filgueira L, Kuster M. Distal extension of the direct anterior approach to the hip poses risk to neurovascular structures: an anatomical study. *J Bone Joint Surg Am* 2015; **97**: 126-132 [PMID: 25609439 DOI: 10.2106/JBJS.N.00551]
 - 17 **Alecci V**, Valente M, Crucil M, Minerva M, Pellegrino CM, Sabbadini DD. Comparison of primary total hip replacements performed with a direct anterior approach versus the standard lateral approach: perioperative findings. *J Orthop Traumatol* 2011; **12**: 123-129 [PMID: 21748384 DOI: 10.1007/s10195-011-0144-0]
 - 18 **Seng BE**, Berend KR, Ajluni AF, Lombardi AV. Anterior-supine minimally invasive total hip arthroplasty: defining the learning curve. *Orthop Clin North Am* 2009; **40**: 343-350 [PMID: 19576401 DOI: 10.1016/j.ocl.2009.01.002]
 - 19 **Barton C**, Kim PR. Complications of the direct anterior approach for total hip arthroplasty. *Orthop Clin North Am* 2009; **40**: 371-375 [PMID: 19576405 DOI: 10.1016/j.ocl.2009.04.004]
 - 20 **Ropars M**, Morandi X, Hutten D, Thomazeau H, Berton E, Darnault P. Anatomical study of the lateral femoral cutaneous nerve with special reference to minimally invasive anterior approach for total hip replacement. *Surg Radiol Anat* 2009; **31**: 199-204 [PMID: 18982237 DOI: 10.1007/s00276-008-0433-3]
 - 21 **Chen LH**, Huang QW, Wang WJ, He ZR, Ding WL. The applied anatomy of anterior approach for minimally invasive hip joint surgery. *Clin Anat* 2009; **22**: 250-255 [PMID: 19089989 DOI: 10.1002/ca.20750]
 - 22 **De Geest T**, Vansintjan P, De Loore G. Direct anterior total hip arthroplasty: complications and early outcome in a series of 300 cases. *Acta Orthop Belg* 2013; **79**: 166-173 [PMID: 23821968]
 - 23 **Leunig M**, Faas M, von Knoch F, Naal FD. Skin crease 'bikini' incision for anterior approach total hip arthroplasty: surgical technique and preliminary results. *Clin Orthop Relat Res* 2013; **471**: 2245-2252 [PMID: 23412730 DOI: 10.1007/s11999-013-2806-0]
 - 24 **Berend KR**, Lombardi AV, Seng BE, Adams JB. Enhanced early outcomes with the anterior supine intermuscular approach in primary total hip arthroplasty. *J Bone Joint Surg Am* 2009; **91** Suppl 6: 107-120 [PMID: 19884418 DOI: 10.2106/JBJS.I.00525]
 - 25 **Keggi KJ**, Huo MH, Zatorski LE. Anterior approach to total hip replacement: surgical technique and clinical results of our first one thousand cases using non-cemented prostheses. *Yale J Biol Med* 1993; **66**: 243-256 [PMID: 8209560]
 - 26 **Matsuura M**, Ohashi H, Okamoto Y, Inori F, Okajima Y. Elevation of the femur in THA through a direct anterior approach: cadaver and clinical studies. *Clin Orthop Relat Res* 2010; **468**: 3201-3206 [PMID: 20405347 DOI: 10.1007/s11999-010-1349-x]
 - 27 **Matta JM**, Shahrardar C, Ferguson T. Single-incision anterior approach for total hip arthroplasty on an orthopaedic table. *Clin Orthop Relat Res* 2005; **441**: 115-124 [PMID: 16330993 DOI: 10.1097/01.blo.0000194309.70518.cb]
 - 28 **Rathod PA**, Bhalla S, Deshmukh AJ, Rodriguez JA. Does fluoroscopy with anterior hip arthroplasty decrease acetabular cup variability compared with a nonguided posterior approach? *Clin Orthop Relat Res* 2014; **472**: 1877-1885 [PMID: 24549773 DOI: 10.1007/s11999-014-3512-2]
 - 29 **Hananouchi T**, Takao M, Nishii T, Miki H, Iwana D, Yoshikawa H, Sugano N. Comparison of navigation accuracy in THA between the mini-anterior and -posterior approaches. *Int J Med Robot* 2009; **5**: 20-25 [PMID: 19107818 DOI: 10.1002/rcs.226]
 - 30 **Kreuzer S**, Leffers K. Direct anterior approach to total hip arthroplasty using computer navigation. *Bull NYU Hosp Jt Dis* 2011; **69** Suppl 1: S52-S55 [PMID: 22035486]
 - 31 **Barton C**, Banga K, Beaulé PE. Anterior Hueter approach in the treatment of femoro-acetabular impingement: rationale and technique. *Orthop Clin North Am* 2009; **40**: 389-395 [PMID: 19576407 DOI: 10.1016/j.ocl.2009.03.002]
 - 32 **Kleinert K**, Werner C, Mamisch-Saupe N, Kalberer F, Dora C. Closed suction drainage with or without re-transfusion of filtered shed blood does not offer advantages in primary non-cemented total hip replacement using a direct anterior approach. *Arch Orthop Trauma Surg* 2012; **132**: 131-136 [PMID: 21874574 DOI: 10.1007/s00402-011-1387-1]

P- Reviewer: Cui Q

S- Editor: Ji FF L- Editor: A E- Editor: Li D



Total elbow arthroplasty is moving forward: Review on past, present and future

Ante Prkić, Christiaan JA van Bergen, Bertram The, Denise Eygendaal

Ante Prkić, Christiaan JA van Bergen, Bertram The, Denise Eygendaal, Department of Orthopedic Surgery, Amphia Hospital, 4800 RK Breda, The Netherlands

Author contributions: Prkić A had written the main part of the article; van Bergen CJA had aided in writing; The B and Eygendaal D had proof-read the article multiple times and have aided in writing.

Conflict-of-interest statement: There is no conflict of interest associated with any of the senior author or other coauthors contributed their efforts in this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Ante Prkić, BSc, Department of Orthopedic Surgery, Amphia Hospital, PO Box 90158, 4800 RK Breda, The Netherlands. aprki@live.nl
Telephone: +31-64-8340436

Received: May 27, 2015

Peer-review started: May 30, 2015

First decision: August 4, 2015

Revised: October 13, 2015

Accepted: November 3, 2015

Article in press: November 4, 2015

Published online: January 18, 2016

been taken to optimize this treatment in order to achieve better post-operative outcomes. To understand these progresses and to discover aspects for upcoming improvements, we present a review on the past developments, the present state of affairs and future developments which may improve patient care further.

Key words: Total elbow arthroplasty; History; Future; Improvements; Review

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Total elbow arthroplasty (TEA) is a relatively uncommon surgical procedure, performed in selected cases of incapacitating elbow diseases. In the past four decades, TEA has evolved from an experimental procedure to a reliable option, which is still more frequently performed. We believe it is necessary to understand the history of the development of TEA in order to accomplish further improvements. In this review we focus on the evolution of the elbow arthroplasty, from a historic overview, up to the present and address issues that could improve the clinical outcome in today's practice.

Prkić A, van Bergen CJA, The B, Eygendaal D. Total elbow arthroplasty is moving forward: Review on past, present and future. *World J Orthop* 2016; 7(1): 44-49 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/44.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.44>

Abstract

The elbow joint is a complex joint, which, when impaired in function, leads to severe disability. In some cases however, an arthroplasty might be an appropriate treatment. In the past four decades, large steps have

INTRODUCTION

From an anthropologic point of view, the upper extremity in humans has evolved into an instrument capable of achieving a large range of motion in order to perform highly complex tasks. This "open kinetic chain"

demands different anatomic structures in comparison to the “closed kinetic chain” of the lower extremity.

Consequently, pathological conditions differ between the two extremities. Pathology of the lower extremity generally results in reduced mobility of the patient. In the upper extremity however, pathologies here restrict the patient from performing simple activities in daily life. In this situation, the problem cannot be managed by the help of external aids (*e.g.*, wheelchairs or crutches)^[1].

The elbow is a complex joint, consisting of three independent joints which cooperate together to move in multiple axes while maintaining a high level of stability^[2]. The humero-ulnar joint permits a flexion/extension motion and is additionally stabilized by the olecranon and coronoid process in extreme flexion and extension. The combination of the proximal and distal radio-ulnar joint allows a pronation/supination movement, which is restricted by ligaments to a certain degree. The flexion of the elbow is important in allowing the hand to reach above and at the level of the head in order to achieve simple, yet important day-to-day activities, such as eating and the washing of hair and face. The combination of these movements, as well as shoulder rotations, allows versatile positioning of the hand in space and is a prerequisite for the fulfillment of complex tasks.

A decreased range of motion in the elbow joint can be directly due to pathology, *i.e.*, primary osteoarthritis, or trauma. Pain, usually secondary to pathology such as rheumatoid arthritis, is another factor that may restrict elbow function as well. A total elbow arthroplasty (TEA) can improve the range of motion and can also relieve pain in selected cases. Therefore, TEA can considerably improve function of the upper limb and increase the quality of life.

Though the use of TEA has almost doubled between 1998 and 2011 in the United States, it is still a relatively uncommon orthopedic procedure. It is performed more often in women than in men^[3] and is also used in relatively young patients^[4,5]. The number of TEA performed annually is 1.4 in 100000 of the population, considerably less than the 70 to 99 in 100000 of the population for total hip replacement^[4,6].

The expanding practice of TEA leads to a new field in orthopedic surgery. We believe it is necessary to understand the history of the development of TEA in order to accomplish further improvements. In this review we will focus on the evolution of the elbow arthroplasty, from a historic overview to the present and address issues that could improve the clinical outcome in today's practice.

THE PAST

The first salvage surgery by excising infected humeral and ulnar bone was performed by Ambroise Pare in the sixteenth century to prevent amputation due to an infected elbow joint^[7]. In the nineteenth century, as more advanced surgical and post-operative care could be provided, creating a pseudoarthrosis by resecting

the distal humerus became an option for incapacitating elbow disease. Following the developments in hip surgery, instead of resecting the joint, the idea of replacing the diseased elbow joint became a concept. It resulted in two streams; the anatomical arthroplasty, aimed to recreate native anatomical structures, and the functional arthroplasty, which covers the functionality of the elbow joint but does not resemble normal anatomical structures.

In 1925, the first attempt to replace an elbow joint by prosthetic materials was documented, when Robineau inserted an anatomically correct elbow prosthesis, consisting of metal and vulcanized rubber. In 1941, Boerema used a hinged non-anatomical prosthesis completely made of metal^[7].

In 1952, Venable^[8] published a case-report of a custom-made anatomical prosthesis after a comminutive fracture of the distal humerus which was not amenable for proper osteosynthesis. A short-term follow-up of 15 mo was reported with a good outcome^[8].

The promising results of experimental elbow surgery led to a rush on patents for elbow arthroplasties by several inventive doctors. In 1954, a functional prosthetic elbow joint was patented by Prevo^[9], but did not reach a widespread use due to frequent loosening. In 1972, Dee^[10] reported his treatment of 12 patients using a functionally designed TEA. This publication initiated an increase in various TEA models in the 1970's, ranging from stemmed devices to anatomy-resembling resurfacing models^[9,11-17]. However, overall post-operative complication rates including; loosening, deep infection, and ulnar nerve neuropathy were high; ranging up to 57%^[18].

It has been a challenge to design a TEA, which copies the native function and stability of all three articulations in the elbow joint. A drawback of anatomical arthroplasties was the lack of intrinsic stability. The anatomical, unlinked resemblance requires the integrity of ligaments and muscles. However, these structures often become insufficient in long-standing disease such as rheumatoid arthritis. Therefore, the unlinked anatomical design has led to a high dislocation rate^[19,20].

During flexion and extension of the elbow, some degrees of valgus and varus laxity is normal^[21]. However, the linked “first generation” TEA's did not offer this laxity, which resulted in frequent loosening due to stress at the implant-bone transition^[18]. This problem was overcome by the “second generation” TEA, introducing sloppy hinges, which allow some varus-valgus laxity due to their semi-constrained design.

Fixation of the prosthesis proved to be challenging too, resulting in the application of a wide range of methods: Prevo^[9] designed screw-threaded stems, Stevens a slide-on self-locking resurfacing arthroplasty, Schlein^[11], Pritchard *et al.*^[13] and Dee^[10] used smooth cemented stems, Roper *et al.*^[14] used a cemented humeral component and Amis and Miller^[16] used screw fixation for the ulnar component^[9,11,13-17]. Harmon^[12] used two rings as a radiocapitellar joint. These models are

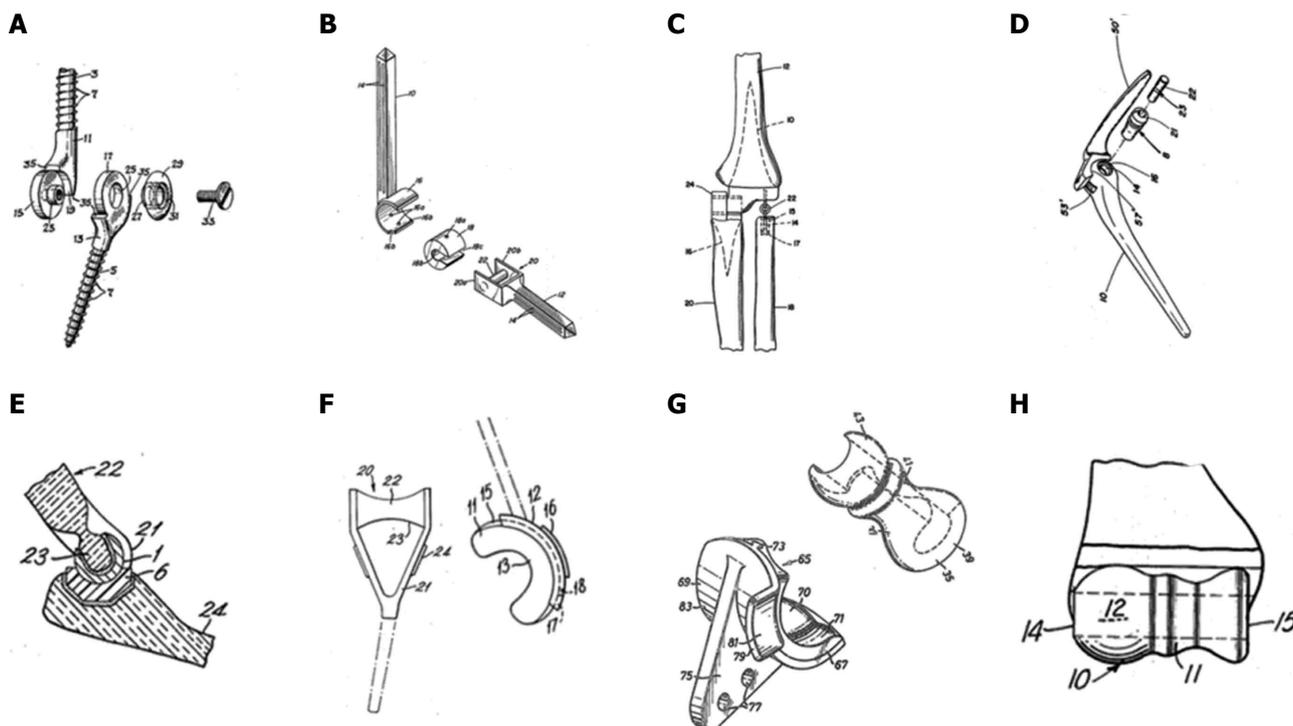


Figure 1 Historical, distinctive types of total elbow arthroplasty. A: Prevo^[9] (1954); B: Schlein^[11] (1974); C: Harmon^[12] (1978); D: Pritchard^[13] (1976); E: Roper^[14] (1975); F: Dee^[15] (1974); G: Amis^[16] (1981); H: Stevens^[17] (1970).

presented in Figure 1.

Beside improvements in materials and models, different operative techniques have arisen, each with their own advantages. In general, two approaches can be distinguished; the triceps sparing and non-triceps sparing approach. The non-triceps sparing approach, entails the triceps tendon to be split longitudinally or reflected from its insertion at the olecranon and at the end of surgery, needs to be repaired, yielding good results^[22].

In the triceps sparing approach, a Chevron osteotomy of the olecranon is performed, distal to the triceps insertion, which is turned aside *en-bloc* with the triceps tendon attached. After insertion of the TEA this Chevron osteotomy is repaired. A study showed the triceps-sparing approach may result in better range of motion and a lower chance of infection compared to the triceps-detaching approach^[23].

The human factor of gained experience on TEA surgery, together with improved materials, has led to positive results regarding clinical outcome and revision rates. Also larger trials and level 4 follow-up data coming from registries have enabled more thorough research on TEA, contributing to evidence-based patient care.

THE PRESENT

In today's practice, the indications for elbow arthroplasty include all kinds of incapacitating elbow diseases, such as primary osteoarthritis, post-traumatic osteoarthritis, rheumatoid arthritis, comminutive elbow fractures, post-traumatic deformities and oncologic disease. However,

unlike in hip and knee arthroplasty, the main indication is not primary osteoarthritis. In 1997, the main indication for TEA in the State of New York, United States, was rheumatoid arthritis. However, in 2006 a shift was seen to trauma as the main indication for TEA^[5].

Today, both the linked sloppy hinged and unlinked TEA's are available. Fixed hinge models are not used contemporarily. According to the patient's pathology and surgeons' preferred choice of the type of implant is often made pre-operatively. A "third generation" type of TEA is currently available, which allows the surgeon to decide during surgery to place a linked or unlinked implant.

Survival rates of different types of TEA have improved in the past four decades to around 90% after 5 years^[24,25]. Cumulative revision rates after four to five years for fixed-hinge models is 13%, for sloppy hinge models 11%, and for unlinked models 13%^[25]. In the short term, the main cause of failure is infection, while in the long term, the main cause is aseptic loosening by prosthetic wear^[25,26]. When compared per group, the fixed-hinge models have a loosening rate of 11%, the sloppy hinged models 5% and the unlinked TEA's 10%^[25].

Deep, periprosthetic infection is a serious complication in arthroplasty surgery, since it requires aggressive treatment in order to preserve the implant without removing it, as well as other problems to patients. To counter the infection rate, the use of pre-operative antibiotics has become standard and maximum aseptic measures are taken during surgery, such as double gloving and laminar flow^[27]. Use of antibiotic-containing bone cement has lowered the deep infection rate to

around 8%^[4,28].

The use of bone cement might play a role in the aseptic loosening rate. A comparative study of cemented and uncemented ulnar components showed a lower rate of loosening in cemented components^[29]. To avoid the use of bone cement and still achieve a firm bone-implant interface, several prosthetic coatings are available. These use the concept of bone ingrowth or osseointegration. The prosthesis is coated with hydroxyapatite, the molecular equivalent of bone. Human osteoclasts can dissolve the coating and attract osteoblasts to replace the coating with human bone^[30]. A different concept is the ability to host osteoblasts in an optimal environment to enhance the intertwining of bone and implant. This can be accomplished with tantalum mesh or titanium beads^[31-33].

To prevent metallosis, which might occur in metal-on-metal articulations, and to minimize shear stress between components, a plastic inlay is used. Depending on the type of arthroplasty, the inlay is either a polyethylene layer between unlinked components (iBP) or a bushing (Discovery, Coonrad-Morrey). These inlays are made of different materials, which aim to minimize wear of the prosthesis.

Wear debris can trigger "particle disease", which in turn leads to arthroplasty component loosening and eventually failure^[34]. Analysis of loosened TEA's showed presence of wear debris (predominantly bone cement, polyethylene and metal) in surrounding tissue, due to wear of the polyethylene interface^[35]. The inlay wear can be lowered by either crosslinking the polymers or adding substances, such as vitamin E^[36,37]. However, no long-term follow-up results are published for elbow arthroplasty.

Patient-reported outcome scales nowadays have a more prominent role in assessing elbow function. Outcome measures have shifted from solely surgeon-opinion, to patient-oriented questionnaires, which focus on activities of daily life^[38]. In a review on outcomes after TEA, the patient-reported outcomes were good or excellent in 78% of cases^[25]. The function assessed by improvement of range of motion, was better in fixed-hinge models and sloppy hinged models (38 degrees and 35 degrees, resp.) than for unlinked models (20 degrees)^[25].

THE FUTURE

Considering the present issues of aseptic loosening and infective complications of elbow arthroplasty, there is obvious room for improvement. Ongoing insights in elbow kinematics might guide implant designers in refining TEA, not only by design but also by choice of material^[21]. The previously mentioned third generation TEA models might provide a good choice when a pre-operative decision on linked or unlinked TEA is not yet clear. Also, restoring the radiocapitellar joint by inserting a radial head prosthesis is possible.

Because of the increasing use of elbow arthroplasties,

an inevitable problem occurs; revision arthroplasty. Because of good results, orthopedic surgeons may perform TEA's with less difficulty in incapacitated patients than several decades ago. Besides, treatment of systemic diseases, such as rheumatoid arthritis has improved, with an overall increase in the quality of life, exposing TEA to a longer period of use. Results on TEA revision are promising; in a recent study revision led to pain relief and improved range of motion after failure of primary TEA^[39].

The improved overall results might also question the need of post-operative functional restrictions, such as restricted lifting activities. These movements lead to shear distracting forces on the bone-implant junction and are therefore theoretical risk factors for implant loosening. In linked TEA types the pulling forces during lifting are transferred more to the humeral component than in unlinked TEA, since unlinked TEA requires ligaments and muscles to remain stable in this situation and is not connected to the ulnar component. However, no studies on post-operative rehabilitation are published, yet high-demanding patients show worse overall implant survival compared to low-demanding patients^[40]. Therefore, research on post-operative management should be conducted to determine both mechanical factors influencing implant survival and optimal functional improvement.

Furthermore, several aspects on TEA research itself should be addressed. By setting up large implant registries, trends in the long-term can be studied. In Scotland, Sweden, Norway, the Netherlands and New Zealand, data on elbow arthroplasties are reported on a routine basis^[4,40,41]. If this could be expanded to more countries, larger cohort studies with better follow-ups are possible^[42]. Large registries also raise the possibility to assess practical questions, for example, a recommended minimum of annual cases to retain optimal surgical results. The Scottish and Finnish arthroplasty registers show that high-volume specialized centers yield better implant survival^[4,40].

Use of pre-operative plain radiographs allows to plan implant size on beforehand, to optimize concordance between the pre-operative native elbow joint and the arthroplasty. Concerning the planning of the implant size, a radiograph-based planning tool is available, with good results in hip and knee arthroplasty. However, even though the intra-observer variability is good, the predictive value of this form of planning is insufficient^[43]. A three-dimensional planning tool would possibly give more accurate information on TEA placement and sizing^[44].

Another question is the use of three-dimensional guiding. Creating three-dimensional structures can be seen in two ways, creating the implant itself or re-creating the diseased elbow. Firstly, unlike Venable described in 1952, patient-specific implants could be made without preceding surgery, according to pre-operative CT-scans. However, on a large scale, this might be too labor-intensive to plan and too expensive to fabricate. Therefore, patient-specific implants could be

used in cases, where usual implants are not suitable.

Secondly, re-creating the diseased elbow could be of beneficial use in complex cases with severe deformation, e.g., the surgeon practicing on a model beforehand. This is already a method used in maxillofacial surgery^[45]. In knee arthroplasty, patient-specific cutting guides, based on pre-operative MRI- or CT-scans, are available for difficult cases^[46-49].

CONCLUSION

The knowledge on elbow arthroplasty has improved greatly in the past seven decades. With more encouraging results and a more widespread awareness, further improvements can be made. By setting up databases on implants, a structured analysis on adverse factors can be made to identify further improvable factors. Advances in materials and technical aids, such as three-dimensional printers, might improve postoperative outcomes.

ACKNOWLEDGMENTS

We would like to thank Robin L Peckitt for his review on English grammar.

REFERENCES

- 1 **de Putter CE**, Selles RW, Haagsma JA, Polinder S, Panneman MJ, Hovius SE, Burdorf A, van Beeck EF. Health-related quality of life after upper extremity injuries and predictors for suboptimal outcome. *Injury* 2014; **45**: 1752-1758 [PMID: 25150751 DOI: 10.1016/j.injury.2014.07.016]
- 2 **Fornalski S**, Gupta R, Lee TQ. Anatomy and biomechanics of the elbow joint. *Tech Hand Up Extrem Surg* 2003; **7**: 168-178 [PMID: 16518218 DOI: 10.1097/00132585-200311010-00001]
- 3 **Singh J**, Ramachandran R. Sex differences in characteristics, utilization, and outcomes of patient undergoing total elbow arthroplasty: a study of the US nationwide inpatient sample. *Clin Rheumatol* 2014 [PMID: 25316506 DOI: 10.1007/s10067-014-2778-9]
- 4 **Jenkins PJ**, Watts AC, Norwood T, Duckworth AD, Rymaszewski LA, McEachan JE. Total elbow replacement: outcome of 1,146 arthroplasties from the Scottish Arthroplasty Project. *Acta Orthop* 2013; **84**: 119-123 [PMID: 23485072 DOI: 10.3109/17453674.2013.784658]
- 5 **Gay DM**, Lyman S, Do H, Hotchkiss RN, Marx RG, Daluiski A. Indications and reoperation rates for total elbow arthroplasty: an analysis of trends in New York State. *J Bone Joint Surg Am* 2012; **94**: 110-117 [PMID: 22257996 DOI: 10.2106/JBJS.J.01128]
- 6 **Lohmander LS**, Engesaeter LB, Herberts P, Ingvarsson T, Lucht U, Puolakka TJ. Standardized incidence rates of total hip replacement for primary hip osteoarthritis in the 5 Nordic countries: similarities and differences. *Acta Orthop* 2006; **77**: 733-740 [PMID: 17068703 DOI: 10.1097/01.NOR.0000284657.70000.5a]
- 7 **Wadsworth TG**. Surgery of arthritis. In: Wadsworth TG, editor. *The Elbow*. Churchill Livingstone, 2008: 303
- 8 **Venable CS**. An elbow and an elbow prosthesis; case of complete loss of the lower third of the humerus. *Am J Surg* 1952; **83**: 271-275 [PMID: 14903376 DOI: 10.1016/0002-9610(52)90255-9]
- 9 **Prevo S**. Prosthetic elbow joint. United States patent US 2696817A, 1954. Available from: URL: <http://www.google.com/patents/US2696817>
- 10 **Dee R**. Total replacement arthroplasty of the elbow for rheumatoid arthritis. *J Bone Joint Surg Br* 1972; **54**: 88-95 [PMID: 5011749]
- 11 **Schlein A**. Prosthesis for total arthroplasty of the elbow joint. United States patent US 3816854A, 1974. Available from: URL: <http://www.google.com/patents/US3816854>
- 12 **Harmon D**. Elbow prosthesis. United States patent US 4129902A, 1978. Available from: URL: <http://www.google.com/patents/US4129902>
- 13 **Pritchard R**, Walker P. Elbow joint prosthesis. United States patent US 3990117A, 1976. Available from: URL: <http://www.google.com/patents/US3990117>
- 14 **Roper B**, Swanson S. Endoprosthetic elbow joint devices. United States patent US 3919725A, 1975. Available from: URL: <http://www.google.com/patents/US3919725>
- 15 **Dee R**. Endoprosthetic elbow joint. United States patent US 3852831A, 1974. Available from: URL: <http://www.google.com/patents/US3852831>
- 16 **Amis A**, Miller J. Elbow prosthesis. United States patent US 4242758A, 1981. Available from: URL: <http://www.google.com/patents/US4242758>
- 17 **Stevens P**. Osteoarticular prosthetic method. United States patent US 3547115A, 1970. Available from: URL: <http://www.google.com/patents/US3547115>
- 18 **Soni RK**, Cavendish ME. A review of the Liverpool elbow prosthesis from 1974 to 1982. *J Bone Joint Surg Br* 1984; **66**: 248-253 [PMID: 6707062]
- 19 **Schreiber JJ**, Warren RF, Hotchkiss RN, Daluiski A. An online video investigation into the mechanism of elbow dislocation. *J Hand Surg Am* 2013; **38**: 488-494 [PMID: 23391358 DOI: 10.1016/j.jhsa.2012.12.017]
- 20 **Voloshin I**, Schippert DW, Kakar S, Kaye EK, Morrey BF. Complications of total elbow replacement: a systematic review. *J Shoulder Elbow Surg* 2011; **20**: 158-168 [PMID: 21134667 DOI: 10.1016/j.jse.2010.08.026]
- 21 **Kincaid BL**, An KN. Elbow joint biomechanics for preclinical evaluation of total elbow prostheses. *J Biomech* 2013; **46**: 2331-2341 [PMID: 23978692 DOI: 10.1016/j.jbiomech.2013.07.027]
- 22 **Tsuge K**, Murakami T, Yasunaga Y, Kanaujia RR. Arthroplasty of the elbow. Twenty years' experience of a new approach. *J Bone Joint Surg Br* 1987; **69**: 116-120 [PMID: 3818716]
- 23 **Dachs RP**, Fleming MA, Chivers DA, Carrara HR, Du Plessis JP, Vretos BC, Roche SJ. Total elbow arthroplasty: outcomes after triceps-detaching and triceps-sparing approaches. *J Shoulder Elbow Surg* 2015; **24**: 339-347 [PMID: 25591460 DOI: 10.1016/j.jse.2014.11.038]
- 24 **Fevang BT**, Lie SA, Havelin LI, Skredderstuen A, Furnes O. Results after 562 total elbow replacements: a report from the Norwegian Arthroplasty Register. *J Shoulder Elbow Surg* 2009; **18**: 449-456 [PMID: 19393935 DOI: 10.1016/j.jse.2009.02.020]
- 25 **Little CP**, Graham AJ, Carr AJ. Total elbow arthroplasty: a systematic review of the literature in the English language until the end of 2003. *J Bone Joint Surg Br* 2005; **87**: 437-444 [PMID: 15795188 DOI: 10.1302/0301-620X.87B4.15692]
- 26 **Throckmorton T**, Zarkadas P, Sanchez-Sotelo J, Morrey B. Failure patterns after linked semiconstrained total elbow arthroplasty for posttraumatic arthritis. *J Bone Joint Surg Am* 2010; **92**: 1432-1441 [PMID: 20516319 DOI: 10.2106/JBJS.I.00145]
- 27 **Ward WG**, Cooper JM, Lippert D, Kablawi RO, Neiberg RH, Sherertz RJ. Glove and gown effects on intraoperative bacterial contamination. *Ann Surg* 2014; **259**: 591-597 [PMID: 24045444 DOI: 10.1097/SLA.0b013e3182a6fd9]
- 28 **Kraay MJ**, Figgie MP, Inglis AE, Wolfe SW, Ranawat CS. Primary semiconstrained total elbow arthroplasty. Survival analysis of 113 consecutive cases. *J Bone Joint Surg Br* 1994; **76**: 636-640 [PMID: 8027155]
- 29 **van der Heide HJ**, de Vos MJ, Brinkman JM, Eygendaal D, van den Hoogen FH, de Waal Malefijt MC. Survivorship of the KUDO total elbow prosthesis--comparative study of cemented and uncemented ulnar components: 89 cases followed for an average of 6 years. *Acta Orthop* 2007; **78**: 258-262 [PMID: 17464616 DOI: 10.1080/174536707100137711]
- 30 **Cook SD**, Thomas KA, Kay JF, Jarcho M. Hydroxyapatite-coated titanium for orthopedic implant applications. *Clin Orthop Relat*

- Res 1988; 225-243 [PMID: 2838208 DOI: 10.1097/00003086-198807000-00030]
- 31 **D'Angelo F**, Murena L, Campagnolo M, Zatti G, Cherubino P. Analysis of bone ingrowth on a tantalum cup. *Indian J Orthop* 2008; **42**: 275-278 [PMID: 19753152 DOI: 10.4103/0019-5413.39553]
- 32 **Kienapfel H**, Sprey C, Wilke A, Griss P. Implant fixation by bone ingrowth. *J Arthroplasty* 1999; **14**: 355-368 [PMID: 10220191 DOI: 10.1016/S0883-5403(99)90063-3]
- 33 **Wazen RM**, Lefebvre LP, Baril E, Nanci A. Initial evaluation of bone ingrowth into a novel porous titanium coating. *J Biomed Mater Res B Appl Biomater* 2010; **94**: 64-71 [PMID: 20336725 DOI: 10.1002/jbm.b.31624]
- 34 **Gallo J**, Goodman SB, Kontinen YT, Raska M. Particle disease: biologic mechanisms of periprosthetic osteolysis in total hip arthroplasty. *Innate Immun* 2013; **19**: 213-224 [PMID: 22751380 DOI: 10.1177/1753425912451779]
- 35 **Day JS**, Baxter RM, Ramsey ML, Morrey BF, Connor PM, Kurtz SM, Steinbeck MJ. Characterization of wear debris in total elbow arthroplasty. *J Shoulder Elbow Surg* 2013; **22**: 924-931 [PMID: 23582703 DOI: 10.1016/j.jse.2013.02.001]
- 36 **Renò F**, Cannas M. UHMWPE and vitamin E bioactivity: an emerging perspective. *Biomaterials* 2006; **27**: 3039-3043 [PMID: 16457883 DOI: 10.1016/j.biomaterials.2006.01.016]
- 37 **Glyn-Jones S**, Isaac S, Hauptfleisch J, McLardy-Smith P, Murray DW, Gill HS. Does highly cross-linked polyethylene wear less than conventional polyethylene in total hip arthroplasty? A double-blind, randomized, and controlled trial using roentgen stereophotogrammetric analysis. *J Arthroplasty* 2008; **23**: 337-343 [PMID: 18358369 DOI: 10.1016/j.arth.2006.12.117]
- 38 **Longo UG**, Franceschi F, Loppini M, Maffulli N, Denaro V. Rating systems for evaluation of the elbow. *Br Med Bull* 2008; **87**: 131-161 [PMID: 18539627 DOI: 10.1093/bmb/ldn023]
- 39 **Plaschke HC**, Thillemann T, Belling-Sørensen AK, Olsen B. Revision total elbow arthroplasty with the linked Coonrad-Morrey total elbow arthroplasty: a retrospective study of twenty procedures. *Int Orthop* 2013; **37**: 853-858 [PMID: 23420324 DOI: 10.1007/s00264-013-1821-9]
- 40 **Skyttä E T**, Eskelinen A, Paavolainen P, Ikävälko M, Remes V. Total elbow arthroplasty in rheumatoid arthritis: a population-based study from the Finnish Arthroplasty Register. *Acta Orthop* 2009; **80**: 472-477 [PMID: 19562563 DOI: 10.3109/17453670903110642]
- 41 **Kärrholm J**. The Swedish Hip Arthroplasty Register (www.shpr.se). *Acta Orthop* 2010; **81**: 3-4 [PMID: 20170435 DOI: 10.3109/17453671003635918]
- 42 **Ayers DC**, Bozic KJ. The importance of outcome measurement in orthopaedics. *Clin Orthop Relat Res* 2013; **471**: 3409-3411 [PMID: 23934032 DOI: 10.1007/s11999-013-3224-z]
- 43 **Pappas ND**, Watson JT, Erickson JM, Baldwin KD, Lee DH. Reliability and accuracy of templating humeral and ulnar components for total elbow arthroplasty. *Am J Orthop* (Belle Mead NJ) 2013; **42**: 321-323 [PMID: 24078944]
- 44 **Fadero PE**, Shah M. Three dimensional (3D) modelling and surgical planning in trauma and orthopaedics. *Surgeon* 2014; **12**: 328-333 [PMID: 24821263 DOI: 10.1016/j.surge.2014.03.008]
- 45 **Torabi K**, Farjood E, Hamedani S. Rapid Prototyping Technologies and their Applications in Prosthodontics, a Review of Literature. *J Dent* (Shiraz) 2015; **16**: 1-9 [PMID: 25759851]
- 46 **Kerens B**, Boonen B, Schotanus M, Kort N. Patient-specific guide for revision of medial unicondylar knee arthroplasty to total knee arthroplasty: beneficial first results of a new operating technique performed on 10 patients. *Acta Orthop* 2013; **84**: 165-169 [PMID: 23496649 DOI: 10.3109/17453674.2013.785908]
- 47 **Zhu M**, Chen JY, Chong HC, Yew AK, Foo LS, Chia SL, Lo NN, Yeo SJ. Outcomes following total knee arthroplasty with CT-based patient-specific instrumentation. *Knee Surg Sports Traumatol Arthrosc* 2015; Epub ahead of print [PMID: 26410097]
- 48 **Asada S**, Mori S, Matsushita T, Nakagawa K, Tsukamoto I, Akagi M. Comparison of MRI- and CT-based patient-specific guides for total knee arthroplasty. *Knee* 2014; **21**: 1238-1243 [PMID: 25199712 DOI: 10.1016/j.knee.2014.08.015]
- 49 **Woolson ST**, Harris AH, Wagner DW, Giori NJ. Component alignment during total knee arthroplasty with use of standard or custom instrumentation: a randomized clinical trial using computed tomography for postoperative alignment measurement. *J Bone Joint Surg Am* 2014; **96**: 366-372 [PMID: 24599197 DOI: 10.2106/JBJS.L.01722]

P- Reviewer: Murata A, Smith GCS
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Review of management of unstable elbow fractures

Omer Ozel, Emre Demircay

Omer Ozel, Emre Demircay, Department of Orthopedic Surgery, Baskent University, 34662 Istanbul, Turkey

Author contributions: All the authors contributed to this paper.

Conflict-of-interest statement: All authors declare that they have no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Emre Demircay, Associate Professor, Department of Orthopedic Surgery, Baskent University, Oymaci Sokak No: 7 Altunizade, 34662 Istanbul, Turkey. emredemircay@hotmail.com
 Telephone: +90-216-5541500
 Fax: +90-216-6519746

Received: June 4, 2015

Peer-review started: June 5, 2015

First decision: July 6, 2015

Revised: October 7, 2015

Accepted: November 3, 2015

Article in press: November 4, 2015

Published online: January 18, 2016

Abstract

Stable and painless elbow motion is essential for activities of daily living. The elbow joint is the second most commonly dislocated joint in adults. The goals of treatment are to perform a stable fixation of all fractures, to achieve concentric and stable reduction of the elbow and to provide early motion. The treatment modality for complex elbow instability is almost always surgical. The treatment objectives are anatomic reduction, stable fixation, and early rehabilitation of the elbow. The common complications of these unstable

fractures include recurrent instability, stiffness, myositis ossificans, heterotopic calcification, and neurovascular dysfunction. We analyzed the management of complex elbow fractures and instabilities on the basis of recent literature and suggested possible guidelines for the treatment in this paper. In conclusion, recognition of the injury pattern and restoration of the joint stability are the prerequisites for any successful treatment of an unstable elbow injury.

Key words: Transolecranon fracture; Coronoid fracture; Monteggia injury; Radial head fracture; Terrible triad

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: As the elbow joint is the second most commonly dislocated joint in adults, we aimed to analyze the management of complex elbow fractures and instabilities, on the basis of recent literature and suggested possible guidelines for the treatment in this paper.

Ozel O, Demircay E. Review of management of unstable elbow fractures. *World J Orthop* 2016; 7(1): 50-54 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/50.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.50>

INTRODUCTION

Basic elbow function requires stable and painless elbow motion. The three articulations, namely the ulnotrochlear, radiocapitellar, and proximal radioulnar joints, provide elbow flexion/extension and supination/pronation. Static and dynamic constraints create stability of the elbow joint. The ulnohumeral articulation, anterior bundle of the medial collateral ligament, and lateral collateral ligament complex form the primary static constraints. The joint capsule and radial head are among the secondary static constraints. The dynamic constraints, such as the common flexor and extensor

muscle groups, are any muscles crossing the elbow joint that exert a compressive force on the joint^[1].

The elbow is the second most commonly dislocated joint in adults^[2]. The dislocations may be complex or simple. When dislocations are associated with fractures, they are designated as complex. The reported annual incidence of simple and complex elbow dislocations is 6.1 per 100000 patients^[3]. Radial head fractures/dislocations, coronoid fractures, terrible triad injuries, transolecranon fracture-dislocations, and Monteggia-like lesions can be listed as common causes of complex elbow injuries.

Complex elbow fractures and instability typically present with edema, tenderness, pain in active/passive movement, and restriction of motion. A fall onto the extended outstretched hand or a direct trauma to the elbow is usually described as the mechanism of the injury. Anteroposterior and lateral standard radiographs and computerized tomography scans (either standard or 3D) are needed to properly evaluate the bone injuries and to accurately plan their surgical treatment. Neurovascular examination and documentation of the injuries before and after any manipulation are of critical importance. A temporary fracture alignment with cast immobilization may be done until definitive surgery in patients with severe injuries.

The treatment modality for complex elbow instability is almost always surgical. The treatment objectives are anatomic reduction, stable fixation, and early rehabilitation of the elbow.

The common complications of these unstable fractures include recurrent instability, stiffness, myositis ossificans, heterotopic calcification, and neurovascular dysfunction.

In this review, we analyze the management of complex elbow fractures and instability on the basis of recent literature, and suggest possible guidelines for the treatment of these injuries.

RADIAL HEAD FRACTURES

Radial head fractures are among the most common elbow fractures, occurring in up to 20% of all elbow injuries^[4]. Radial head fractures are mostly associated with complex injuries like elbow dislocation, and lateral collateral ligament (LCL) and medial collateral ligament (MCL) tears. Impaction fractures of the capitellum may also be associated with radial head fractures, and can easily be overlooked^[5]. Only about 5% of cases have a radial head fracture as an isolated injury^[6,7]. In a large incidence study^[8], the mean age was found to be 36 years and the female-to-male ratio was 47.7/53.3. A thorough physical examination is essential to diagnose associated ligament injuries. Fluoroscopy may be used to confirm an MCL injury if medial pain and ecchymosis are present. If the MCL is injured, the role of the radial head in valgus resistance increases up to 30%^[9,10]. Stable anatomic reconstruction of the radial head is the primary objective of the treatment.

The Mason classification system^[11] divided radial head fractures into three categories: type I, non-displaced fractures; type II, displaced partial head fractures; and type III, comminuted displaced fractures involving the whole head.

Modifications to the Mason classification were introduced to guide treatment. The Hotchkiss modification^[12] defines type I fractures as non-displaced fractures (< 2 mm displacement) without mechanical blockage that do not require surgery, type II fractures as displaced fractures (> 2 mm displacement) of the radial head or neck that lack severe comminution, may have mechanical blockage to movement, and usually require open reduction and internal fixation, and type III fractures as severely comminuted fractures of the radial head and neck. Satisfactory reconstructions of these fractures are not possible, and therefore the radial head is either excised or replaced with a prosthesis^[13]. Fragment excision is avoided in complex elbow instability to prevent valgus instability^[14]. If there is an associated LCL rupture, it should be repaired after appropriate management of the radial head fracture, either by fixation or by prosthetic replacement. Suture anchors or transosseous sutures can be used for the reconstruction. The joint stability should be confirmed by dynamic fluoroscopic examination. If residual instability persists, MCL reconstruction and/or dynamic elbow fixation should be done^[15,16].

CORONOID FRACTURES

The coronoid process plays a pivotal role as an anterior buttress in providing elbow stability. Although coronoid fractures may occur in isolation, they are more commonly seen as a component of unstable elbow fractures^[17].

The classification proposed by Moon *et al.*^[18], which defines anteromedial facet lesions, may be better for guiding the surgical management of coronoid fractures. Type I injuries involve fractures of the coronoid tip, and are divided into two subtypes based on the fracture size. Subtype 1 fractures are smaller than 2 mm, and subtype 2 fractures are larger than 2 mm. In type II injuries, the anteromedial aspect of the coronoid is fractured. These injuries are divided into three subtypes based on the anatomic location. Subtype 1 fractures involve the rim, subtype 2 fractures involve the rim and the tip, and subtype 3 fractures involve the rim and the sublime tubercle with or without the tip. Type III fractures are basal coronoid fractures involving at least 50% of the height of the coronoid. They are divided into two subtypes depending on whether the fracture involves the base of the olecranon. Stable fixation and ligament repair are essential for the treatment of coronoid fractures^[19,20].

TERRIBLE TRIAD INJURIES

Terrible triad injuries have the most common complex pattern. They comprise a radial head fracture and elbow

Table 1 Reviewed studies investigating unstable elbow fracture diagnosis and treatment

Author	Ring <i>et al</i> ^[16]	Chemama <i>et al</i> ^[22]	Konrad <i>et al</i> ^[26]	Mouhsine <i>et al</i> ^[29]	Zeiders <i>et al</i> ^[21]	Winter <i>et al</i> ^[13]	Mortazavi <i>et al</i> ^[30]	Strauss <i>et al</i> ^[27]
Year	2002	2010	2007	2007	2008	2009	2006	2006
Mean age (range)	36 (17-62)	46 (26-75)	42.1 (21-72)	54 (22-82)	NA	40 (18-77)	35 (22-58)	UHD+: 46.8 UHD-: 55
n (female/male)	56 (21/35)	23 (7-16)	63 (22/41)	14 (8/6)	32 (NA)	13 (4/9)	8 (1/7)	UHD+: 6 (2/4) UHD-: 17 (12/5)
Radial fracture Mason classification	Type 2: 30 Type 3: 26	Type 1: 2 Type 2: 9 Type 3: 10 Radial neck: 2	Type 2: 7 Type 3: 9	NA	NA	13 non-reperable RH fracture	Type 1: 1 Type 3: 1	Type 1: 1 Type 2: 2 Type 3: 3 UHD+: Type 1: 4 Type 2: 6 (UHD+) Type 2: 17 (UHD-) NA
Coronoid fracture classification R-M	NA	Type 1: 16 Type 2: 7	NA	NA	NA	Type 1: 5 Type 2-3: 8	Type 3: 4	UHD+: Type 1: 4 Type 2: 6 (UHD+) Type 2: 17 (UHD-) NA
Monteggia fracture classification (BADO)	NA	NA	Type 1: 19 Type 2: 37 Type 3: 5 Type 4: 2	NA	NA	NA	NA	Type 2: 6 (UHD+) Type 2: 17 (UHD-) NA
Time to surgery	NA	NA	First 24 h	NA	NA	1.9 d (1-4)	3.8 d	NA
Monteggia fracture Ulna treatment	NA	NA	Bado 1, 3, 4 (26 3.5 mm DCP) Bado 2 (26 plate, 11 tension band)	NA	NA	NA	NA	UHD+: Small fragment plates UHD-: Small fragment plates NA
Transolecranon fracture treatment	NA	NA	NA	K-wire and tension band: 7 3.5 mm 1/3 plate: 2 3.5 mm DCP: 1 3.5 mm recon. plate: 4	NA	NA	3.5 mm AO recons. Plate: 7 K-wire and tension band: 1	NA
Coronid treatment	NA	None: 10 TOS: 3 Anchor: 2 Screw: 4 Plate: 1 Resection: 3	Lag screws through the ulnar plate or indirect repositioning	NA	32 patients repair of coronoid brachialis Complex pull-through suture tec	NA	4 patients interfragmentary Screws through the plate	UHD+: Type 3 (lag screws)
Radial head treatment	Mason 2: 26 (screw), 4 (plate, screw) Mason 3: 22 (plate, screw), 4 (screw)	13 mini screws Radial neck: 2 plate RHP: 4 PRHR: 2 TRHR: 2	46 luxation CR 12 RH ORIF 4 RH resection	NA	6-intact RH 7-reconst 19-prothesis	13 RHP	1 type 1: Mini screws 1 type 3: Total excision RH	Type 1, 2: mini fragment plates Type 3: 3 replacement
LCL repair	NA	NA	NA	None	18 (anchor) 12 (mcl + lcl rep)	No: 4 abs suture Used for repair	NA	UHD+: 6
MCL repair	NA	NA	NA	None	2 (ancor) 12 (mcl + lcl rep)	NA	NA	UHD+: 0
External fixator	NA	None	NA	None	21 hinged ex-fix	NA	NA	UHD+: 1 hinged ex-fix
Follow-up	48 mo	63 mo	8.4 yr (5-14) (47 patients)	42 mo (7-84)	3 yr (1-5)	25 mo (15-48)	37.4 mo (10-50)	UHD+: 28 mo (14-48) UHD-: 29 (12-60)
Range of motion	MFA Mason 2: 119 Mason 3: 111	MFA: 109 MSA: 64 MPA: 70	MFA: 97.5 MFR: 125	MFA: 103 MSA: 76 MPA: 68	MFA: 100	MFA: 120	MFA: 93 MFR: 157.5	UHD+: MFA 95, MSA 55, MPA 50 UND-: MFA 122, MSA 67, MPA 60

Mean score	Mason 2: MEPS: 87 (75-100) BM: 92 Mason 3: BM: 86	14 patients result	BM: 87.2 (45-100) DASH: 17.4 (0-70)	BM: 82 (78-100)	DASH: 23 (19/28)	BM: 86.5 (55-100)	BM: 88 (71-100) ASES: 89 (69-100)	UHD+: DASH 34 (0-80), BM: 73.8 UHD-: DASH 23 (0-70), BM: 83
Unsatisfactory	Mason 2: 4 Mason 3: 14	BM: 0	BM: (9 fair) (4 poor) result	BM: 2 fair 2 poor		2 (stiffness, infection)	BM: 1 fair	UHD+: 2 UHD-: 7

NA: Not applicable; UHD: Ulnohumeral dislocation; RH: Radial head; R-M: Roger Morrey; DCP: Dynamic compression plate; TOS: Transosseous suture; RHP: Radial head prosthesis; PRHR: Partial radial head resection; TRHR: Total radial head resection; MFA: Mean flexion arch; MSA: Mean supination arch; MPA: Mean pronation arch; MFR: Mean forearm rotation; BM: Broberg and Morrey index; MEPS: Mayo elbow performance score; DASH: Disabilities of the arm shoulder and hand; ASES: American Shoulder and Elbow Surgeons assessment system; LCL: Lateral collateral ligament; MCL: Medial collateral ligament.

dislocation along with a coronoid fracture. Both medial and lateral compartments can be exposed through a posterior incision. The Kocher approach can be used for the radial head fracture. Hotchkiss type I and type II radial head fractures can be fixed with headless screws or a plate^[12]. Prosthetic replacement is mandatory for comminuted radial head fractures (type III) to avoid chronic instability. There is often a comminuted type 1 fracture in the coronoid, and it can usually only be fixed with a transosseous suture. If there is an isolated fragment that is sufficiently large, fixation with K wires or screws can be done^[19]. The LCL is repaired last, and elbow stability is assessed by fluoroscopy. In the presence of a residual instability, the MCL should also be repaired or a hinged external fixator should be applied^[7,21,22] (Table 1).

MONTEGGIA-LIKE LESIONS

Monteggia injuries comprise a fracture of the ulnar shaft with an associated radial head dislocation. Monteggia originally described the lesions as a fracture of the proximal third of the ulna and an anterior dislocation of the proximal epiphysis of the radius^[23]. Bado^[23] classified these injuries by primarily focusing on the radial component. Jupiter *et al*^[24] modified this classification by defining subtypes for the posterior Monteggia lesions (Bado type 2). Ulnohumeral dislocation, radial fracture, proximal and/or distal radioulnar dislocation, and interosseous membrane lesions may also accompany the ulnar fracture and radiohumeral dislocation. Each of these must be recognized and treated. The varying combinations of these injured structures explains the complexity and diversity of the management procedures.

Anatomic reduction and stabilization of the ulna and the ulnohumeral joint is the primary objective of surgical treatment for posterior elbow fracture-dislocations^[25]. The radial head fracture is addressed initially. If the radial head cannot be salvaged satisfactorily, radial head arthroplasty is preferred. To size the radial head properly, the ulnar length should be restored by a provisional fixation^[17]. The coronoid process is stabilized after the ulnar shaft fracture has been addressed, and the olecranon is fixed with a dorsal plate. Finally, ligamentous components of the injury are addressed^[26,27] (Table 1).

TRANSOLECRANON FRACTURE-DISLOCATIONS (ANTERIOR OLECRANON FRACTURE-DISLOCATIONS)

The radial head is dislocated anteriorly with an associated olecranon fracture in this injury pattern^[28]. Two subtypes have been described: One with a simple olecranon fracture, and one with a comminuted olecranon fracture^[28]. The second subtype is more common and may be associated with trochlear and coronoid fractures. This injury pattern is distinct from the anterior Monteggia (Bado type 1) lesion, because in transolecranon fracture-dislocation, the ulnohumeral stability is lost but the radioulnar relationship remains intact. Bony disruption is the main reason for the failure of the ulnohumeral joint rather than the ligamentous structures.

Anatomic reduction with particular attention to restoring the ulnar length and greater sigmoid notch is essential in the treatment^[29] (Table 1). Restoration of the ulnohumeral anatomy is crucial to prevent radiocapitellar instability or subluxation^[25,30] (Table 1).

CONCLUSION

Surgical treatments of complex elbow fracture dislocations are among the most challenging procedures for orthopedic surgeons. Interpretation of the underlying mechanisms for elbow instability and accurate identification of the injured structures are crucial for surgical planning. Stable elbow fracture fixation is important for early elbow motion and avoiding joint stiffness. Recognition of the injury pattern and restoration of the joint stability are the prerequisites for any successful treatment of an unstable elbow injury.

In this review, we have examined the diagnosis, classification, and treatment of unstable elbow fractures. Future studies should be conducted to determine the optimal management strategies, the role of ligament reconstruction, and reductions in the complication rate.

REFERENCES

- 1 Parsons BO, Ramsey ML. Elbow instability and reconstruction. In: Flynn JM. Orthopaedic knowledge update. Rosemont, IL: American Academy of Orthopaedic Surgeons, 2011: 343-351

- 2 **Kuhn MA**, Ross G. Acute elbow dislocations. *Orthop Clin North Am* 2008; **39**: 155-161, v [PMID: 18374806 DOI: 10.1016/j.ocl.2007.12.004]
- 3 **Josefsson PO**, Nilsson BE. Incidence of elbow dislocation. *Acta Orthop Scand* 1986; **57**: 537-538 [PMID: 3577725 DOI: 10.3109/17453678609014788]
- 4 **Glaser DL**, Armstrong AD. Elbow and forearm trauma. In: Flynn JM. Orthopaedic knowledge update. Rosemont, IL: American Academy of Orthopaedic Surgeons, 2011: 325-341
- 5 **Nalbantoglu U**, Gereli A, Kocaoglu B, Aktas S, Turkmen M. Capitellar cartilage injuries concomitant with radial head fractures. *J Hand Surg Am* 2008; **33**: 1602-1607 [PMID: 18984344 DOI: 10.1016/j.jhsa.2008.05.016]
- 6 **van Riet RP**, Morrey BF, O'Driscoll SW, Van Glabbeek F. Associated injuries complicating radial head fractures: a demographic study. *Clin Orthop Relat Res* 2005; **441**: 351-355 [PMID: 16331026 DOI: 10.1097/01.blo.0000180606.30981.78]
- 7 **Ring D**, Jupiter JB, Zilberfarb J. Posterior dislocation of the elbow with fractures of the radial head and coronoid. *J Bone Joint Surg Am* 2002; **84-A**: 547-551 [PMID: 11940613]
- 8 **Kovar FM**, Jaindl M, Thalhammer G, Rupert S, Platzer P, Endler G, Vielgut I, Kutscha-Lissberg F. Incidence and analysis of radial head and neck fractures. *World J Orthop* 2013; **4**: 80-84 [PMID: 23610756 DOI: 10.5312/wjo.v4.i2.80]
- 9 **Søjbjerg JO**, Ovesen J, Nielsen S. Experimental elbow instability after transection of the medial collateral ligament. *Clin Orthop Relat Res* 1987; **(218)**: 186-190 [PMID: 3568478]
- 10 **Morrey BF**, Tanaka S, An KN. Valgus stability of the elbow. A definition of primary and secondary constraints. *Clin Orthop Relat Res* 1991; **(265)**: 187-195 [PMID: 2009657]
- 11 **Mason ML**. Some observations on fractures of the head of the radius with a review of one hundred cases. *Br J Surg* 1954; **42**: 123-132 [PMID: 13209035 DOI: 10.1002/bjs.18004217203]
- 12 **Hotchkiss RN**. Displaced Fractures of the Radial Head: Internal Fixation or Excision? *J Am Acad Orthop Surg* 1997; **5**: 1-10 [PMID: 10797202]
- 13 **Winter M**, Chuinard C, Cikes A, Pelegri C, Bronsard N, de Peretti F. Surgical management of elbow dislocation associated with non-reparable fractures of the radial head. *Chir Main* 2009; **28**: 158-167 [PMID: 19356963 DOI: 10.1016/j.main.2009.02.003]
- 14 **Duckworth DG**, Avakian Z, Chien C. Newly defined fracture pattern specific to Mason III radial head fractures: fracture description, management and outcomes using screw fixation. *ANZ J Surg* 2012; **82**: 434-438 [PMID: 22548755 DOI: 10.1111/j.1445-2197.2012.06094.x]
- 15 **Tan V**, Daluiski A, Capo J, Hotchkiss R. Hinged elbow external fixators: indications and uses. *J Am Acad Orthop Surg* 2005; **13**: 503-514 [PMID: 16330512]
- 16 **Ring D**, Quintero J, Jupiter JB. Open reduction and internal fixation of fractures of the radial head. *J Bone Joint Surg Am* 2002; **84-A**: 1811-1815 [PMID: 12377912]
- 17 **Giannicola G**, Sacchetti FM, Greco A, Cinotti G, Postacchini F. Management of complex elbow instability. *Musculoskelet Surg* 2010; **94** Suppl 1: S25-S36 [PMID: 20383679 DOI: 10.1007/s12306-010-0065-8]
- 18 **Moon JG**, Zobitz ME, An KN, O'Driscoll SW. Optimal screw orientation for fixation of coronoid fractures. *J Orthop Trauma* 2009; **23**: 277-280 [PMID: 19318871 DOI: 10.1097/BOT.0b013e31819df8c9]
- 19 **Budoff JE**. Coronoid fractures. *J Hand Surg Am* 2012; **37**: 2418-2423 [PMID: 23101539 DOI: 10.1016/j.jhsa.2012.09.002]
- 20 **Garrigues GE**, Wray WH, Lindenhovius AL, Ring DC, Ruch DS. Fixation of the coronoid process in elbow fracture-dislocations. *J Bone Joint Surg Am* 2011; **93**: 1873-1881 [PMID: 22012524 DOI: 10.2106/JBJS.I.01673]
- 21 **Zeiders GJ**, Patel MK. Management of unstable elbows following complex fracture-dislocations--the "terrible triad" injury. *J Bone Joint Surg Am* 2008; **90** Suppl 4: 75-84 [PMID: 18984720 DOI: 10.2106/JBJS.H.00893]
- 22 **Chemama B**, Bonneville N, Peter O, Mansat P, Bonneville P. Terrible triad injury of the elbow: how to improve outcomes? *Orthop Traumatol Surg Res* 2010; **96**: 147-154 [PMID: 20417913 DOI: 10.1016/j.otsr.2009.11.009]
- 23 **Bado JL**. The Monteggia lesion. *Clin Orthop Relat Res* 1967; **50**: 71-86 [PMID: 6029027 DOI: 10.1097/00003086-196701000-00008]
- 24 **Jupiter JB**, Leibovic SJ, Ribbans W, Wilk RM. The posterior Monteggia lesion. *J Orthop Trauma* 1991; **5**: 395-402 [PMID: 1761999 DOI: 10.1097/00005131-199112000-00003]
- 25 **Scolaro JA**, Beingessner D. Treatment of monteggia and transolecranon fracture-dislocations of the elbow: A critical analysis review. *JBJS Reviews* 2014; **2**: e3 [DOI: 10.2106/JBJS.RVW.M.00049]
- 26 **Konrad GG**, Kundel K, Kreuz PC, Oberst M, Sudkamp NP. Monteggia fractures in adults: long-term results and prognostic factors. *J Bone Joint Surg Br* 2007; **89**: 354-360 [PMID: 17356149 DOI: 10.1302/0301-620X.89B3.18199]
- 27 **Strauss EJ**, Tejwani NC, Preston CF, Egol KA. The posterior Monteggia lesion with associated ulnohumeral instability. *J Bone Joint Surg Br* 2006; **88**: 84-89 [PMID: 16365126 DOI: 10.1302/0301-620X.88B1.16704]
- 28 **Biga N**, Thomine JM. Trans-olecranal dislocations of the elbow. *Rev Chir Orthop Reparatrice Appar Mot* 1974; **60**: 557-567 [PMID: 4282168]
- 29 **Mouhsine E**, Akiki A, Castagna A, Cikes A, Wettstein M, Borens O, Garofalo R. Transolecranon anterior fracture dislocation. *J Shoulder Elbow Surg* 2007; **16**: 352-357 [PMID: 17188909 DOI: 10.1016/j.jse.2006.07.005]
- 30 **Mortazavi SM**, Asadollahi S, Tahririan MA. Functional outcome following treatment of transolecranon fracture-dislocation of the elbow. *Injury* 2006; **37**: 284-288 [PMID: 16442109 DOI: 10.1016/j.injury.2005.10.028]

P- Reviewer: Garg B, Malik H

S- Editor: Gong XM L- Editor: A E- Editor: Li D



Calcific tendinitis of the rotator cuff

Mohamed Taha ElShewy

Mohamed Taha ElShewy, Orthopedic Department, Cairo University, Cairo 11412, Egypt

Author contributions: ElShewy MT solely contributed to this work.

Conflict-of-interest statement: There is no conflict of interest associated with the sole author or others who contributed their efforts in this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Mohamed Taha ElShewy, MD, Orthopedic Department, Cairo University, 51 Demascus street, Dokki, Cairo 11412, Egypt. mshewy@gmail.com
Telephone: +20-12-22281698
Fax: +20-2-37496759

Received: May 26, 2015

Peer-review started: May 28, 2015

First decision: August 22, 2015

Revised: September 5, 2015

Accepted: November 17, 2015

Article in press: November 25, 2015

Published online: January 18, 2016

Abstract

Calcific tendinitis within the rotator cuff tendon is a common shoulder disorder that should be differentiated from dystrophic calcification as the pathogenesis and natural history of both is totally different. Calcific tendinitis usually occurs in the fifth and sixth decades of life among sedentary workers. It is classified into formative and resorptive phases. The chronic formative phase results from transient hypoxia that is commonly

associated with repeated microtrauma causing calcium deposition into the matrix vesicles within the chondrocytes forming bone foci that later coalesce. This phase may extend from 1 to 6 years, and is usually asymptomatic. The resorptive phase extends from 3 wk up to 6 mo with vascularization at the periphery of the calcium deposits causing macrophage and mononuclear giant cell infiltration, together with fibroblast formation leading to an aggressive inflammatory reaction with inflammatory cell accumulation, excessive edema and rise of the intra-tendineous pressure. This results in a severely painful shoulder. Radiological investigations confirm the diagnosis and suggest the phase of the condition and are used to follow its progression. Although routine conventional X-ray allows detection of the deposits, magnetic resonance imaging studies allow better evaluation of any coexisting pathology. Various methods of treatment have been suggested. The appropriate method should be individualized for each patient. Conservative treatment includes pain killers and physiotherapy, or "minimally invasive" techniques as needling or puncture and aspiration. It is almost always successful since the natural history of the condition ends with resorption of the deposits and complete relief of pain. Due to the intolerable pain of the acute and severely painful resorptive stage, the patient often demands any sort of operative intervention. In such case arthroscopic removal is the best option as complete removal of the deposits is unnecessary.

Key words: Rotator cuff; Calcific tendinitis; Prevalence; Pathogenesis; Natural history; Classification; Clinical picture; Imaging; Treatment

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This review article discuss calcific tendinitis of the rotator cuff regarding the definition, prevalence, pathology, pathogenesis, natural history, clinical presentation, classification, diagnosis and various treatment modalities.

ElShewy MT. Calcific tendinitis of the rotator cuff. *World J Orthop* 2016; 7(1): 55-60 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/55.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.55>

INTRODUCTION

Calcium deposits within the rotator cuff tendon is a common shoulder disorder^[1]. Calcium deposits may be in the form of calcific tendinitis or dystrophic calcification.

Calcific tendinitis is calcification within a viable and well vascularized rotator cuff. It occurs within the midsubstance of the cuff, 1 to 2 cm proximal to its insertion. Classically, the condition will end by spontaneous resolution and it is uncommon to see other signs of degenerative changes^[2].

Dystrophic calcification is calcification within a non-viable and poorly vascularized rotator cuff. It occurs at the insertion site or at the edges of a cuff tear. Classically, the condition worsens by time and it is common to see other signs of degenerative changes^[2].

PREVALANCE

Calcific tendinitis usually occurs during the fifth and sixth decades of life. It occurs within the supraspinatus tendon in almost 50% of cases. It is more common in females (60%). It occurs more commonly with sedentary workers than with heavy labor workers (45% are house wives)^[3-5].

PATHOGENESIS AND NATURAL HISTORY

Controversy exists over the exact cause of calcific tendinitis. Burkhead^[6] and Gohlke^[7] proposed that it is a degenerative process that involves necrotic changes of tendon fibers that progress into dystrophic calcification.

Mclaughlin^[8] believed that it proceeded from focal hyalinization of the fibers that become fibrillated and detached from the tendon, thus wounding up into rice-like bodies that later undergo calcification.

On the other hand, Uththoff^[9] pointed out that this may be true regarding dystrophic calcification. But regarding calcific tendinitis they believed that this explanation was most unlikely. They argued that calcific tendinitis occurred in viable and well vascularized tissues and thus could not be a degenerative process, instead they suggested that it was a reparative process progressing through a predictable disease cycle^[9-12].

The calcium deposits may have a chalk-like consistency or a fluid consistency or a mixed one^[13].

CLASSIFICATION AND CLINICAL PRESENTATION

Many classifications have been suggested to describe

calcific tendinitis. Some classified it according to the severity of the symptoms into acute, subacute and chronic^[14]. Others classified it according to the radiological form into two categories. The first with localized, discrete, dense and homogenous deposits with spontaneous healing tendency and the second with diffuse, fluffy and heterogeneous deposits characterized by delayed and slow healing^[15]. The French society of arthroscopy divided the condition into four types: Type A (20%) with homogenous deposits with well defined edges; Type B (45%) with heterogeneous fragmented deposits with well defined edges; Type C (30%) with heterogeneous deposits with ill defined edges and Type D which is not calcific tendinitis but degenerative dystrophic calcifications at the rotator cuff insertion^[16].

Uththoff *et al*^[12] were the ones who described the complete cycle of the calcium deposits and explained the development of its natural history. They divided the condition into formative and resorptive phases. Lying within the two phases most authors motioned the presence of three stages; pre-calcification (silent), calcification (impingement) and post-calcification (acute)^[17-20].

The chronic formative phase results from transient hypoxia that is commonly associated with repeated microtrauma and sometimes with a significant single trauma. This results in increased proteoglycan levels that induce tenocyte metaplasia into chondrocytes. This is followed by calcium deposits, mainly into the matrix vesicles within the chondrocytes. These deposits develop into bone foci that later coalesce.

During the acute resorptive phase the periphery of the calcium deposits shows vascularization with macrophage and mononuclear giant cell infiltration together with fibroblast formation. This produces an aggressive inflammatory reaction with inflammatory cell accumulation, excessive edema and rise of the intratendineous pressure. This leads to severe pain which is attributed by some to secondary impingement resulting from the increased tendon size, or due to rupture of the deposits into the subacromial space or into the bursa.

During the post-calcification stage the fibroblasts lay down collagen (mainly type II) that fills the gap. This will mature into collagen type I within 12 to 16 mo^[9,11,12].

The clinical presentation is highly variable and depends on the phase the patient is passing through. During the chronic formative phase that may extend anywhere from 1 to 6 years, the patient may be completely asymptomatic. In some cases the condition will only be discovered accidentally. Some patients may present with symptoms that mimic mild impingement. However during the acute resorptive phase, the patient usually presents with severe symptoms that may extend from 3 wk up to 6 mo. In general, the more severe the symptoms are, the shorter the duration of the condition is. The patient presents with tremendous pain all over the shoulder with tenderness over the supraspinatus insertion. Pain commonly extends to the root of the neck

with difficulty during overhead activity associated with muscle spasm. It is very difficult to perform any of the special tests due to the unbearable pain.

IMAGING

Radiological investigations confirm the diagnosis and may even make the diagnosis in asymptomatic cases. It also suggests the phase of the condition and is used to follow its progression.

They include conventional X-ray in true antero-posterior, lateral and outlet views. Deposits within the subscapularis may be detected by anteroposterior view in external rotation. In internal rotation, the deposits within the infraspinatus and teres minor may be detected. "Skullcap appearance" indicate rupture of the deposits within the bursa^[21].

Ultrasonographic examination was reported to be more sensitive in detecting the calcium deposits within the cuff^[22].

Computed tomography allowed better localization of the deposits^[21]. Although routine conventional X-ray allowed detection of the deposits, magnetic resonance imaging (MRI) studies allow better evaluation of any coexisting pathology. The deposits present with a low intensity signal in the T1 weighted images. In the T2 weighted images there may be perifocal low intensity signal denoting surrounding edema^[23].

The thinned out cuff lateral to the deposits may be falsely interpreted as a cuff tear. MRI arthrography was more beneficial to avoid such false conclusions^[23].

TREATMENT

Various methods of treatment have been suggested. The appropriate method should be individualized for each patient depending on proper understanding of the pathophysiology and natural history of the condition, as well as proper clinical and radiological assessment of the patient, and finally accurate determination of the stage at which the patient presents.

The treatment may be "conservative" including pain killers and physiotherapy, or "minimally invasive" as needling and puncture and aspiration, or "operative" whether arthroscopic or open.

Due to the intolerable pain of the acute and severely painful resorptive stage, the patient often demands any sort of intervention despite explaining to him that the condition is probably resolving.

Since the natural history of the condition ends with resorption of the deposits and complete relief of pain, usually conservative measures are successful in most of cases, reaching 80% in some studies and even 99% in others^[12,24].

During the acute stage the aim is to relief of pain. The efficacy of non-steroidal drugs may be doubtful with frequent need to narcotic medications.

Physiotherapy

Some authors suggested physiotherapy including range of motion exercises to avoid gleno-humeral stiffness and idiopathic frozen shoulder. However there is no evidence that calcific tendinitis causes gleno-humeral capsular contracture^[25].

There is no solid evidence that different physical modalities including infrared, ultrasound, or deep heat have any effect on the natural history of the condition.

Extracorporeal shock wave

Extracorporeal shock wave (ECSW) has been used to treat symptomatic patients passing through the chronic formative phase with definite radiological evidence of calcium deposits^[26].

Most authors report short term symptomatic improvement^[27]. But ECSW was not free from complications, that included transient bone marrow edema and even reported cases of humeral head necrosis^[28,29].

Most authors reported that the improvement is dose dependant, with better results following one or two sessions of high energy applications^[30].

Needling or puncture and lavage

Minimally invasive techniques include needling or puncture and aspiration. These techniques were suggested by many authors aiming at decompressing the deposits and thus relieving the pain. They suggested that direct puncture of the deposits would shorten the natural history of the condition and accelerate resorption in 50% of cases^[31].

Since the fifties of the last century some authors recommended blind needling of the deposits with intralesional local anesthetic injection reporting pain relief in 85% of cases. They reported that the amount of deposits removed didn't affect the outcome and accordingly concluded that pierce opening of the deposits was the essential step and not the calcium removal^[32,33]. In the sixties Depalma and Kruper^[14] popularized blind needling of the deposits without any radiological localization, with good results. Clement reported pain relief within 24 h following repeated blind needling of the deposits (15 to 20 times), after local anesthetic and corticosteroid injection into the subacromial space. He referred the patients to ultrasonic treatment within a few days. He claimed that this would cause active hyperemia that would enhance deposit absorption^[34]. Most authors reported very good results after performing needling under fluoroscopic and, or ultrasonographic guidance^[35,36].

Local corticosteroid injection (whether intralesional or into the subacromial space) following the needling of the deposits, is recommended by some authors with good results and some suggested two or more injections. Many studies showed no evidence that corticosteroid injection improved the results^[36,37]. Some reported that corticosteroids injection was short acting and only symptomatic. Other surgeons argued that corticosteroids

would reduce the tendon healing process^[38]. Neer^[39] disagreed with this claim.

Many authors recommended dual needling and lavage for cases with calcium deposits^[40-42]. Needling is no new technique as it has been described over a century ago by Flint in 1913 as reported by Codman in 1934^[6].

After all of the various needling techniques the patient should be instructed to rest the shoulder for a short period (1 to 2 d) followed by gradual return to daily activities.

The patient should also be forewarned that a successful full recovery may take 3 to 6 mo. During the chronic formative stage the symptoms are usually mild and no intervention is needed. Yet some authors suggested needling (whether blind needling or under radiological guidance) suggesting that direct puncture of the deposits would shorten the natural history of the condition and accelerate deposits resorption^[43]. Non-steroidal drugs may be used every now and then.

The true debate concerning needling or puncture and lavage is the fact that the acute and severe symptoms are almost always associated with an expedient resolution of the condition. Thus, any form of treatment at this point will ultimately be a "success".

Operative intervention

Indications: Many authors suggested that the indications for operative intervention include progression of symptoms that interferes with the daily activities after failure of conservative measures^[44,45].

Neer stated that operative indications include long standing symptoms after failure of conservative measures in the presence of multiple, hard and gritty deposits. He rarely resorted to operative intervention and suggested that residual tendinopathy would follow^[39].

Most authors starting from Burkhead^[6], passing through Lippmann^[1], to Mclaughlin^[8], and up till today^[45,46] agree that surgical removal of rotator cuff calcium deposits end with good permanent results. They agree that the indications include symptomatic patients after failure of conservative measures with radiological evidence of relatively homogenous calcium deposits.

During the resorptive stage, conservative measures were recommended as the natural history of the condition would end with complete resolution of the deposits and the symptoms. Yet operative intervention is to be considered upon the patient's demand due to the intolerable pain despite the conservative measures.

Open surgery: It is performed through a deltoid splitting incision, the site of which may be modified to allow the best access to the exact location of the deposits. The deltoid fibers are separated and the deposits are split-open along the direction of the cuff fibers. Usually the deposits are readily apparent as a bulge within the cuff. The deposits commonly burst out when opened. Open surgery has a high success rate in complete removal of the calcium deposits but with some intraoperative

complications^[47-49]. Some authors suggested resuturing of the cuff if a significant gap is left behind. The benefit of this step is unclear^[13,50]. This is followed by a period of shoulder rest (5 to 7 d), with gradual return to daily activities over a 4 to 6 wk period of time.

Most authors reported that complete intraoperative removal of the deposits was unnecessary as it didn't significantly affect the final clinical outcome. Thus total removal was not essential and sometimes not possible without substantial damage to the tendon^[49,51]. In most cases partial removal of the deposits will finally lead to total resorption. This was reinforced by other studies^[46,52].

Arthroscopic management: Nowadays, open surgery is rarely used to remove calcium deposits as arthroscopy offers a much better choice.

Arthroscopic calcium deposits removal was quite effective, although it may fail to completely remove the deposits compared with open surgery^[47-49]. But as long as complete removal of the deposits was unnecessary, then arthroscopic removal was clearly a better option. Studies showed that the rate of full-thickness rotator cuff tears after calcium deposits removal was quite low (3.9% after a 9-year follow-up)^[53]. Accordingly, rotator cuff repair following calcium deposits removal was not mandatory. However, it was found that the intraoperative status of the rotator cuff had a significant influence on the functional results at follow-up^[47]. In one study, the 2 patients of the 54 cases of the study (3.7%) who needed later rotator cuff repair showed obvious degeneration of the rotator cuff during the removal of the deposits. Accordingly, it should be recommended to repair the rotator cuff after the removal of calcium deposits, whenever the cuff appears to be noticeably degenerative^[46].

Arthroscopic subacromial bursectomy should be performed to allow better visualization of the rotator cuff. In cases with shoulder impingement, subacromial decompression (acromioplasty) should be performed. The calcium deposits were identified as a bulge within the cuff tendon "calcific bulging sign"^[51]. Then, *via* a lateral working portal, a half-moon arthroscopy knife may be used to open up the deposits along the fibers of the cuff. After that, a 3.5-mm motorized shaver was used to remove as much as possible of each deposit, only stopping short of causing any iatrogenic damage to the cuff.

REFERENCES

- 1 Lippmann RK. Observations concerning the calcific cuff deposit. *Clin Orthop* 1961; **20**: 49-60 [PMID: 13762581]
- 2 Uthoff HK, Sarkar K. Classification and definition of tendinopathies. *Clin Sports Med* 1991; **10**: 707-720 [PMID: 1934093]
- 3 Louwerens JK, Sierevelt IN, van Hove RP, van den Bekerom MP, van Noort A. Prevalence of calcific deposits within the rotator cuff tendons in adults with and without subacromial pain syndrome: clinical and radiologic analysis of 1219 patients. *J Shoulder Elbow Surg* 2015; **24**: 1588-1593 [PMID: 25870115 DOI: 10.1016/

- j.jse.2015.02.024]
- 4 **Diehl P**, Gerdesmeyer L, Gollwitzer H, Sauer W, Tischer T. [Calcific tendinitis of the shoulder]. *Orthopade* 2011; **40**: 733-746 [PMID: 21814884 DOI: 10.1007/s00132-011-1817-3]
 - 5 **Oliva F**, Via AG, Maffulli N. Calcific tendinopathy of the rotator cuff tendons. *Sports Med Arthrosc* 2011; **19**: 237-243 [PMID: 21822107 DOI: 10.1097/JSA.0b013e318225bc5f]
 - 6 **Burkhead WZ**. A history of the rotator cuff before Codman. *J Shoulder Elbow Surg* 2011; **20**: 358-362 [PMID: 21397790 DOI: 10.1016/j.jse.2011.01.002]
 - 7 **Gohlke F**. Early European contributions to rotator cuff repair at the turn of the 20th century. *J Shoulder Elbow Surg* 2011; **20**: 352-357 [PMID: 21397789 DOI: 10.1016/j.jse.2011.01.001]
 - 8 **McLaughlin HL**. The selection of calcium deposits for operation; the technique and results of operation. *Surg Clin North Am* 1963; **43**: 1501-1504 [PMID: 14090194]
 - 9 **Uthoff HK**. Calcifying tendinitis, an active cell-mediated calcification. *Virchows Arch A Pathol Anat Histol* 1975; **366**: 51-58 [PMID: 804757 DOI: 10.1007/BF00438677]
 - 10 **Uthoff HK**, Sarkar K. An algorithm for shoulder pain caused by soft-tissue disorders. *Clin Orthop Relat Res* 1990; **(254)**: 121-127 [PMID: 2182249 DOI: 10.1097/00003086-199005000-00018]
 - 11 **Uthoff HK**, Sarkar K, Maynard JA. Calcifying tendinitis: a new concept of its pathogenesis. *Clin Orthop Relat Res* 1976; **(118)**: 164-168 [PMID: 954272 DOI: 10.1097/00003086-197607000-00030]
 - 12 **Uthoff HK**, Loehr JW. Calcific Tendinopathy of the Rotator Cuff: Pathogenesis, Diagnosis, and Management. *J Am Acad Orthop Surg* 1997; **5**: 183-191 [PMID: 10797220]
 - 13 **Gazielly DF**, Bruyere G, Gleyze P, Thomas T. Open acromioplasty with excision of calcium deposits and tendon suture. In: Gazielly DF, Bruyere G, Gleyze P, Thomas T, editors. *The cuff Paris*: Elsevier, 1997: 172-175
 - 14 **Depalma AF**, Kruper JS. Long-term study of shoulder joints afflicted with and treated for calcific tendinitis. *Clin Orthop* 1961; **20**: 61-72 [PMID: 13721957]
 - 15 **Patte D**, Goutallier D. [Periarthritis of the shoulder. Calcifications]. *Rev Chir Orthop Reparatrice Appar Mot* 1988; **74**: 277-278 [PMID: 3187100]
 - 16 **Molé D**, Kempf JF, Gleyze P, Rio B, Bonomet F, Walch G. [Results of endoscopic treatment of non-broken tendinopathies of the rotator cuff. 2. Calcifications of the rotator cuff]. *Rev Chir Orthop Reparatrice Appar Mot* 1993; **79**: 532-541 [PMID: 8085035]
 - 17 **Rowe CR**. Calcific tendinitis. *Instr Course Lect* 1985; **34**: 196-198 [PMID: 3833939]
 - 18 **Booth RE**, Marvel JP. Differential diagnosis of shoulder pain. *Orthop Clin North Am* 1975; **6**: 353-379 [PMID: 1093085]
 - 19 **Re LP**, Karzel RP. Management of rotator cuff calcifications. *Orthop Clin North Am* 1993; **24**: 125-132 [PMID: 8421605]
 - 20 **Diehl P**, Schauwecker J. [Calcific tendinitis of the shoulder: operative and nonoperative treatment options]. *MMW Fortschr Med* 2014; **156**: 56-59; quiz 60 [PMID: 25417477 DOI: 10.1007/s15006-014-3098-3]
 - 21 **Izadpanah K**, Jaeger M, Maier D, Südkamp NP, Ogon P. Preoperative planning of calcium deposit removal in calcifying tendinitis of the rotator cuff - possible contribution of computed tomography, ultrasound and conventional X-Ray. *BMC Musculoskelet Disord* 2014; **15**: 385 [PMID: 25413969 DOI: 10.1186/1471-2474-15-385]
 - 22 **Filippucci E**, Delle Sedie A, Riente L, Di Geso L, Carli L, Caccarelli F, Sakellariou G, Iagnocco A, Grassi W. Ultrasound imaging for the rheumatologist. XLVII. Ultrasound of the shoulder in patients with gout and calcium pyrophosphate deposition disease. *Clin Exp Rheumatol* 2013; **31**: 659-664 [PMID: 24050142]
 - 23 **Loew M**, Sabo D, Wehrle M, Mau H. Relationship between calcifying tendinitis and subacromial impingement: a prospective radiography and magnetic resonance imaging study. *J Shoulder Elbow Surg* 1996; **5**: 314-319 [PMID: 8872930 DOI: 10.1016/S1058-2746(96)80059-0]
 - 24 **Scibek JS**, Carcia CR. Presentation and conservative management of acute calcific tendinopathy: a case study and literature review. *J Sport Rehabil* 2012; **21**: 334-342 [PMID: 22388055]
 - 25 **Matsen FA**, Lippitt SB, Sidles JA, Harrymann D. Synthesis: practice guide lines. In: *Practical evaluation in management of the shoulder*. Philadelphia: WB Saunders, 1994: 221-230
 - 26 **Galasso O**, Amelio E, Riccelli DA, Gasparini G. Short-term outcomes of extracorporeal shock wave therapy for the treatment of chronic non-calcific tendinopathy of the supraspinatus: a double-blind, randomized, placebo-controlled trial. *BMC Musculoskelet Disord* 2012; **13**: 86 [PMID: 22672772 DOI: 10.1186/1471-2474-13-86]
 - 27 **Rebuzzi E**, Coletti N, Schiavetti S, Giusto F. Arthroscopy surgery versus shock wave therapy for chronic calcifying tendinitis of the shoulder. *J Orthop Traumatol* 2008; **9**: 179-185 [PMID: 19384483 DOI: 10.1007/s10195-008-0024-4]
 - 28 **Liu HM**, Chao CM, Hsieh JY, Jiang CC. Humeral head osteonecrosis after extracorporeal shock-wave treatment for rotator cuff tendinopathy. A case report. *J Bone Joint Surg Am* 2006; **88**: 1353-1356 [PMID: 16757772 DOI: 10.2106/JBJS.E.00868]
 - 29 **Durst HB**, Blatter G, Kuster MS. Osteonecrosis of the humeral head after extracorporeal shock-wave lithotripsy. *J Bone Joint Surg Br* 2002; **84**: 744-746 [PMID: 12188497 DOI: 10.1302/0301-620X.84B5.12282]
 - 30 **Bannuru RR**, Flavin NE, Vaysbrot E, Harvey W, McAlindon T. High-energy extracorporeal shock-wave therapy for treating chronic calcific tendinitis of the shoulder: a systematic review. *Ann Intern Med* 2014; **160**: 542-549 [PMID: 24733195 DOI: 10.7326/M13-1982]
 - 31 **Moutounet J**, Chevrot A, Wybier M, Godefroy D. [X-ray guided puncture-aspiration of refractory calcifications of the shoulder]. *Ann Radiol (Paris)* 1992; **35**: 156-159 [PMID: 1288379]
 - 32 **Psaki CG**, Carroll J. Acetic acid ionization; a study of determine the absorptive effects upon calcified tendinitis of the shoulder. *Phys Ther Rev* 1955; **35**: 84-87 [PMID: 13236513]
 - 33 **Friedman MS**. Calcified tendinitis of the shoulder. *Am J Surg* 1957; **94**: 56-61 [PMID: 13424871 DOI: 10.1016/0002-9610(57)90618-9]
 - 34 **Clement BL**. Shoulder bursitis with calcification. *Am J Orthop* 1966; **8**: 160-161 [PMID: 5981438]
 - 35 **Gatt DL**, Charalambous CP. Ultrasound-guided barbotage for calcific tendonitis of the shoulder: a systematic review including 908 patients. *Arthroscopy* 2014; **30**: 1166-1172 [PMID: 24813322 DOI: 10.1016/j.arthro.2014.03.013]
 - 36 **Castillo-González FD**, Ramos-Álvarez JJ, Rodríguez-Fabián G, González-Pérez J, Calderón-Montero J. Treatment of the calcific tendinopathy of the rotator cuff by ultrasound-guided percutaneous needle lavage. Two years prospective study. *Muscles Ligaments Tendons J* 2014; **4**: 220-225 [PMID: 25332939]
 - 37 **de Witte PB**, Selten JW, Navas A, Nagels J, Visser CP, Nelissen RG, Reijnen M. Calcific tendinitis of the rotator cuff: a randomized controlled trial of ultrasound-guided needling and lavage versus subacromial corticosteroids. *Am J Sports Med* 2013; **41**: 1665-1673 [PMID: 23696211 DOI: 10.1177/0363546513487066]
 - 38 **Uthoff HK**, Sarkar K. Calcifying Tendinitis. In: Rockwood CA, Matsen FA, editors. *The Shoulder*. Philadelphia: WB Saunders, 1994: 774-790
 - 39 **Neer CS**. Less frequent procedures. In: Neer CS, editor. *Shoulder reconstruction*. Philadelphia: WB Saunders, 1990: 427-433
 - 40 **Giacomini P**, Siliotto R. [Echo-guided percutaneous treatment of chronic calcific tendinitis of the shoulder]. *Radiol Med* 1999; **98**: 386-390 [PMID: 10780220]
 - 41 **Scanfienza LM**, Viganò S, Martini C, Aliprandi A, Randelli P, Serafini G, Sardanelli F. Double-needle ultrasound-guided percutaneous treatment of rotator cuff calcific tendinitis: tips & amp; tricks. *Skeletal Radiol* 2013; **42**: 19-24 [PMID: 22710923 DOI: 10.1007/s00256-012-1462-x]
 - 42 **Farin PU**, Jaroma H, Soimakallio S. Rotator cuff calcifications: treatment with US-guided technique. *Radiology* 1995; **195**: 841-843 [PMID: 7754018 DOI: 10.1148/radiology.195.3.7754018]
 - 43 **Louwerens JK**, Sierevelt IN, van Noort A, van den Bekerom MP. Evidence for minimally invasive therapies in the management of chronic calcific tendinopathy of the rotator cuff: a systematic

- review and meta-analysis. *J Shoulder Elbow Surg* 2014; **23**: 1240-1249 [PMID: 24774621 DOI: 10.1016/j.jse.2014.02.002]
- 44 **Gschwend N**, Patte D, Zippel J. [Therapy of calcific tendinitis of the shoulder]. *Arch Orthop Unfallchir* 1972; **73**: 120-135 [PMID: 5078902 DOI: 10.1007/BF00415901]
- 45 **Maier M**, Krauter T, Pellengahr C, Schulz CU, Trouillier H, Anetzberger H, Refior HJ. [Open surgical procedures in calcifying tendinitis of the shoulder - concomitant pathologies affect clinical outcome]. *Z Orthop Ihre Grenzgeb* 2002; **140**: 656-661 [PMID: 12476390 DOI: 10.1055/s-2002-36033]
- 46 **El Shewy MT**. Arthroscopic removal of calcium deposits of the rotator cuff: a 7-year follow-up. *Am J Sports Med* 2011; **39**: 1302-1305 [PMID: 21350066 DOI: 10.1177/0363546510396320]
- 47 **Ark JW**, Flock TJ, Flatow EL, Bigliani LU. Arthroscopic treatment of calcific tendinitis of the shoulder. *Arthroscopy* 1992; **8**: 183-188 [PMID: 1637430 DOI: 10.1016/0749-8063(92)90034-9]
- 48 **Porcellini G**, Paladini P, Campi F, Paganelli M. Arthroscopic treatment of calcifying tendinitis of the shoulder: clinical and ultrasonographic follow-up findings at two to five years. *J Shoulder Elbow Surg* 2004; **13**: 503-508 [PMID: 15383805 DOI: 10.1016/j.jse.2004.04.001]
- 49 **Brochon MJ**, Buissière J, Chemtob C, Chaumeil JC. [Rheological study of fluid agar media]. *Ann Pharm Fr* 1983; **41**: 139-150 [PMID: 6651162 DOI: 10.1016/j.arthro.2006.01.012]
- 50 **Litchman HM**, Silver CM, Simon SD, Eshragi A. The surgical management of calcific tendinitis of the shoulder. An analysis of 100 consecutive cases. *Int Surg* 1968; **50**: 474-479 [PMID: 5724542]
- 51 **Rupp S**, Seil R, Kohn D. [Tendinosis calcarea of the rotator cuff]. *Orthopade* 2000; **29**: 852-867 [PMID: 11142905 DOI: 10.1007/s001320050533]
- 52 **Hofstee DJ**, Gosens T, Bonnet M, De Waal Malefijt J. Calcifications in the cuff: take it or leave it? *Br J Sports Med* 2007; **41**: 832-835 [PMID: 17957023 DOI: 10.1136/bjism.2007.036939]
- 53 **Clavert P**, Sirveaux F. [Shoulder calcifying tendinitis]. *Rev Chir Orthop Reparatrice Appar Mot* 2008; **94**: 336-355 [PMID: 19046691 DOI: 10.1016/j.rco.2008.09.010]

P- Reviewer: Drosos GI
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D



Case Control Study

Patient specific guides for total knee arthroplasty are ready for primetime

Martijn GM Schotanus, Bert Boonen, Nanne P Kort

Martijn GM Schotanus, Bert Boonen, Nanne P Kort, Department of Orthopaedic Surgery, Zuyderland Medical Centre, 6162 BG Sittard-Geleen, The Netherlands

Author contributions: Schotanus MGM designed the study, gathered and analysed all the data, wrote the initial draft of the manuscript, managed and performed the study; Boonen B ensured the accuracy of the data and the analysis and gave critical revisions related to important intellectual content of the manuscript; Kort NP designed the study, revised the manuscript and gave final approval of the version of the article to be published.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board (METC Atrium-Orbis-Zuyd, Heerlen, the Netherlands) file name 13-N-09.

Informed consent statement: All patients gave informed consent prior to the study enrolment.

Conflict-of-interest statement: Dr. Nanne P Kort is a consultant on the PSG technique for Biomet, Europe. The other authors declare that they have no conflict of interest.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Martijn GM Schotanus, MSc, Research Manager, Department of Orthopaedic Surgery, Zuyderland Medical Centre, location Dr. H vd Hoffplein 1, 6162 BG Sittard-Geleen, The Netherlands. martijnschotanus@hotmail.com
Telephone: +31-88-4597433
Fax: +31-88-4597986

Received: February 11, 2015

Peer-review started: February 12, 2015

First decision: June 18, 2015

Revised: October 22, 2015

Accepted: November 17, 2015

Article in press: November 25, 2015

Published online: January 18, 2016

Abstract

AIM: To present the radiological results of total knee arthroplasty (TKA) with use of patient specific matched guides (PSG) from different manufacturer in patients suffering from severe osteoarthritis of the knee joint.

METHODS: This study describes the results of 57 knees operated with 4 different PSG systems and a group operated with conventional instrumentation ($n = 60$) by a single surgeon. The PSG systems were compared with each other and subdivided into cut- and pin PSG. The biomechanical axis [hip-knee-ankle angle (HKA)], varus/valgus of the femur [frontal femoral component (FFC)] and tibia (frontal tibial component) component, flexion/extension of the femur [flexion/extension of the femur component (LFC)] and posterior slope of the tibia [lateral tibial component (LTC)] component were evaluated on long-leg standing and lateral X-rays. A percentage of $> 3^\circ$ deviation was seen as an outlier.

RESULTS: The inter class correlation coefficient (ICC) revealed that radiographic measurements between both assessors were reliable ($ICC > 0.8$). Fisher exact test was used to test differences of proportions. The percentage of outliers of the HKA-axis was comparable between both the PSG and conventional groups (12.28% vs 18.33%, $P < 0.424$) and the cut- and pin PSG groups (14.3% vs 10.3%, $P < 1.00$). The percentage of outliers of the FFC (0% vs 18.33%, $P < 0.000$), LFC (15.78% vs 58.33%, $P < 0.000$) and LTC (15.78% vs 41.67%, $P < 0.033$) were significant different in favour of the PSG

group. There were no significant differences regarding the outliers between the individual PSG systems and the PSG group subdivided into cut- and pin PSG.

CONCLUSION: PSG for TKA show significant less outliers compared to the conventional technique. These single surgeon results suggest that PSG are ready for primetime.

Key words: Total knee arthroplasty; Patient specific matched guides; Patient matched instruments; Single surgeon; Alignment; Conventional instruments; Cutting guides; Pin guides

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Total knee arthroplasty (TKA) is one of the most successful and commonly performed surgical procedure for the treatment of severe knee osteoarthritis with excellent 15-20 years survivorships. This article provides an analysis on patient specific matched guides (PSG) between different manufacturers and the conventional technique and between pin- and cutting guides for TKA. In addition, we compared our results with previous studies (level 1 evidence), which are generally unambiguous, and show no radiological difference. However, in this trial, we do see difference in favour of the PSG technique.

Schotanus MGM, Boonen B, Kort NP. Patient specific guides for total knee arthroplasty are ready for primetime. *World J Orthop* 2016; 7(1): 61-68 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/61.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.61>

INTRODUCTION

Total knee arthroplasty (TKA) has been developed significantly over the last decades. Many changes have been made to improve both survival and functioning. A good postoperative biomechanical axis is one of the key elements for a good implant survival. Malalignment is associated with poor implant survivorship^[1-4]. Several studies reported results of postoperative malalignment using conventional intramedullary alignment rods in TKA^[5-9]. Computer navigation was introduced to cope with malalignment and instability in conventionally placed prostheses^[10]. These days, revolutionary changes within the elective knee arthroplasty have taken place due to industry driven interventions^[11]. Patient specific matched guides (PSG) for TKA is a relatively new technique to align the knee prosthesis, using 3D rapid prototyped disposable cut or pin guides that fits on the native anatomy of the individual patient^[12,13]. This perioperative guiding technique eliminates the use of intra- and extra medullary rods to make bony resections. Previous published results on PSG suggest this to be a

good alternative to conventional instrumentation with comparable results, improved radiological outcome and reduced operation time and blood loss^[7,13-23].

This prospective study on PSG between different manufacturers and conventional technique for the implantation of TKA was designed to address the following research questions: Is there a significant difference in outliers in alignment in the frontal and lateral plane between PSG and conventional TKA, secondly between the four individual different PSG systems and thirdly between cut- and pin PSG? We hypothesise that there will be fewer outliers with PSG TKA compared to conventional TKA without differences between different PSG systems and cut- and pin PSG.

MATERIALS AND METHODS

Patients were operated for TKA with PSG systems from 4 different manufactures (Table 1). In daily practice the TKA system and PSG from the company Biomet is used. Between May 2013 and April 2014, 60 consecutive patients with debilitating osteoarthritis (OA) of the knee joint, who were eligible for primary TKA were included (Figure 1). Patients who were not eligible to undergo magnetic resonance imaging (MRI) due to metal artefacts around the knee joint from previous surgery, claustrophobia, movement artefacts during MRI scanning time, pigmented villonodular synovitis, implanted electronic devices and patients that refused to consent were excluded. TKA surgery was done using PSG and consisted of guides from 4 different TKA suppliers (Table 1). The conventional TKA group consisted of 60 patients who were randomly selected from a cohort ($n \geq 500$) as a comparison group. We did not match patients (*e.g.*, body mass index, gender, age and severity of OA) to avoid selection bias.

All patients gave informed consent to participate in this prospective study and were operated by a senior knee orthopaedic surgeon (NK) with extensive experience with PSG^[15,16]. Patients were not blinded to the type of alignment method used. Three patients were excluded from the study and therefore did not receive the intervention as planned. A flowchart of the study design is shown in Figure 2. There were no significant differences in baseline demographics, as summarized in Table 2.

PSG and the conventional TKA surgery are extensively described in previous published studies^[15,16]. Preoperative, a virtual 3 dimensional plan was made based on the imaging protocols of the different manufacturers (Table 1). Preferred component position of the prosthesis was planned to obtain a neutral biomechanical axis [hip-knee-ankle angle (HKA)] and position of the femoral [frontal femoral component (FFC)] and tibial [frontal tibial component (FTC)] components in the frontal plane. All settings during planning in the lateral plane were similar for all PSG systems: Femoral component flexion [flexion/extension of the femur component (LFC)] and tibial component posterior slope

Table 1 Different industries with brand names, guide type, implant name and scanning modality

	Dupuy-Synthes	Smith and Nephew	Zimmer	Biomet
PSG	Trumatch	Visionaire	PSI	Signature
Guides	Cut	Cut	Pin	Pin
Implant	Sigma CR	Genesis II	NexGen	Vanguard CR
Imaging protocol	CT ¹	MRI ²	CT or MRI ¹	CT or MRI ¹

¹Scan of the hip, knee and ankle joint; ²MRI of the knee joint with long leg standing X-ray. PSI: Patient-specific instrument; PSG: Patient specific matched guides; CT: Computed tomography; MRI: Magnetic resonance imaging; CR: Computed radiography.

Table 2 Baseline demographics per alignment method, *n* (%)

	Trumatch	Visionaire	PSI	Signature	Conventional	<i>P</i> value
Number of patients	15	13	14	15	60	
Mean age, yr (range)	72 (57-90)	72 (63-82)	69 (52-86)	68 (56-74)	65 (50-83)	0.097
Male	6 (40)	7 (54)	7 (50)	7 (47)	34 (57)	0.967
Mean BMI (range)	30 (23-36)	30 (23-37)	30 (26-36)	30 (23-38)	28 (21-37)	0.373
Severity OA						
Moderate	13 (87)	11 (85)	13 (93)	14 (93)	53 (88)	0.991
Severe	2 (13)	2 (15)	1 (7)	1 (7)	7 (12)	0.959

PSI: Patient-specific instrument; BMI: Body mass index; OA: Osteoarthritis.

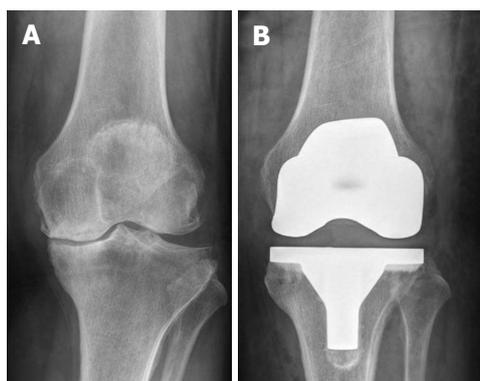


Figure 1 Anterior-posterior radiograph of a left knee of a female patient. A: Preoperative severe osteoarthritis; B: Postoperative with the Sigma CR, total knee arthroplasty (Depuy) *in situ*.

[lateral tibial component (LTC)] were set at 3°. The final approval of settings was done by the operating surgeon (NK). After approval, the disposable cut or pin guides (Table 1) for perioperative alignment were manufactured and used during surgery. A midline approach was used and a cemented prosthesis implemented in all cases (Table 1). The guides were designed to make contact with osteophytes and therefore it was not allowed to remove these prior to the bony cuts. The same procedure was performed in the conventional group, except for the standard conventional rods for femur and tibia with the same implant as the Signature group (Vanguard Complete Knee System, Biomet, Warsaw, INC). Conventional rods were used to align the position of the cutting blocks: LFC and LTC were set at 0°.

All patients received a multimodal pain protocol including spinal or general anesthesia and local infil-

tration analgesia without a drain and urine catheter. Postoperative procedures were the same in all TKA patients. Patients followed an enhanced recovery pathway and received subcutaneous thromboprophylaxis (Fondaparinux) once daily for 35 d, starting on the evening on the first postoperative day.

Preoperative approved planning for the femur and tibia component were compared with the postoperative achieved alignment of each component on radiographs. HKA-axis and implant position were measured with a calibrated protocol on digital images on a PACS system^[15,16]. HKA angle was evaluated on standardized 1-year postoperative frontal long-leg standing X-rays. Varus/valgus position of the FFC and FTC perpendicular to the HKA angle were measured on the same frontal radiographs. Flexion/extension of the LFC, measured from the anterior femoral cortex and posterior or anterior slope of the LTC measured from the posterior cortex of the tibia, were evaluated on 1-year postoperative lateral radiographs. Deviations of > 3° between preoperative planned HKA-axis (sum of FFC and FTC) and individual components (FFC, FTC, LFC and LTC) compared to the postoperative achieved alignment on radiographs, were considered as outliers. Mean values, SD and percentages of > 3° deviation of the preoperative planned alignment and postoperative alignment were first compared between the complete PSG group and the conventional group and all PSG groups were compared with each other. A comparison between cut- and pin guides was also made (Table 1).

Ethical approval

This study was approved by the institutional review board (IRB Atrium-Orbis Zuyd Heerlen, the Netherlands;

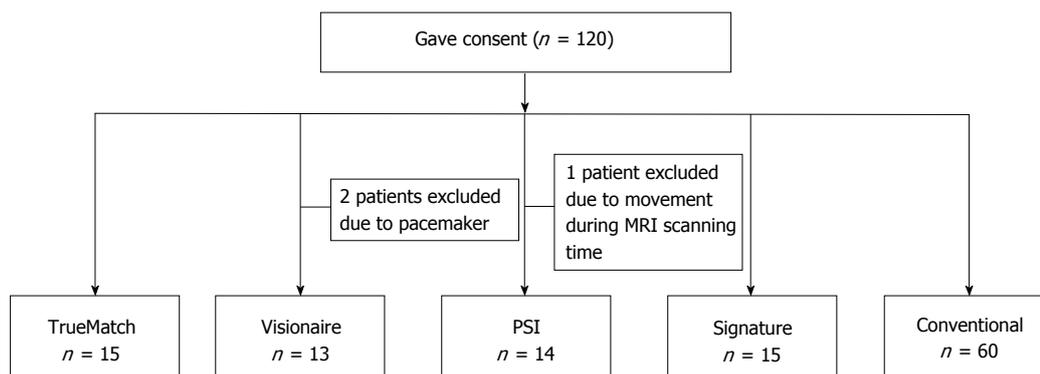


Figure 2 Flowchart study design. PSI: Patient-specific instrument; MRI: Magnetic resonance imaging.

Table 3 Inter observer correlation coefficients

	HKA	FFC	FTC	LFC	LTC
Inter CC	0.811	0.879	0.883	0.850	0.943

HKA: Hip-knee-ankle angle; FFC: Frontal femoral component; FTC: Frontal tibial component; LFC: Flexion/extension of the femur component; LTC: Lateral tibial component; CC: Class correlation coefficient.

IRB-nr.13N09), registered online at the Dutch Trial Register (NTR4739) and was performed in compliance with the Helsinki Declaration of 1975, as revised in 2000. All patients were informed and they consented to providing data for anonymous use.

Statistical analysis

Statistical Package for the Social Sciences V17.0 (SPSS, Inc., Chicago, IL) for Windows was used. All radiographic evaluation was performed once for each radiograph, performed by 2 independent assessors (MS and SH). Inter class correlation coefficient (ICC) was calculated to check for inter observer reliability. An ICC ≥ 0.7 was considered as good correlation. Statistically significant differences for radiographs were analyzed with a one-way ANOVA. The Bonferroni method for correcting for multiple comparisons was used to reduce the chances of obtaining false-positive results (type I errors). Fisher exact test was used to test differences of proportions. P-value was considered to be statistically significant at P ≤ 0.05 for all statistical analyses.

RESULTS

Of the 120 patients included, 3 patients could not be scanned with MRI and were operated with use of computed tomography (CT)-based PSG (Signature, Biomet). Baseline demographics are shown in Table 2. All guides fitted well during the time of operation, there were no conversions to conventional instrumentation. All radiographic measurements of both observers were reliable and ICC's were excellent (Table 3).

With regard to the individual components, percentage of outliers of the FFC (P < 0.000), LFC (P < 0.000) and LTC (P < 0.05) were significantly different

Table 4 Mean (SD) values and amount of patients and percentages of outliers of > 3° deviation of the planned alignment and postoperative alignment compared between the patient specific matched guides and the conventional group, n (%)

Outliers	PSG	Conventional	P value
HKA outliers	7 (12.28)	11 (18.33)	0.424
Mean (SD)	179.49 (2.24)	178.54 (2.27)	0.015
FFC outliers	0 (0)	11 (18.33)	0.000
Mean (SD)	89.44 (1.73)	88.03 (1.73)	0.000
FTC outliers	1 (1.75)	0 (0)	1.000
Mean (SD)	89.87 (1.32)	90.37 (1.38)	0.058
LFC outliers	9 (15.78)	35 (58.33)	0.000
Mean (SD)	86.09 (2.86)	86.04 (3.14)	0.314
LTC outliers	9 (15.78)	25 (41.67)	0.033
Mean (SD)	92.86 (2.64)	87.43 (2.63)	0.000

PSG: Patient specific matched guides; HKA: Hip-knee-ankle angle; FFC: Frontal femoral component; FTC: Frontal tibial component; LFC: Flexion/extension of the femur component; LTC: Lateral tibial component.

in favour of the PSG group (Table 4). Regarding the individual different PSG systems, the mean (SD) HKA-axis (P < 0.000), the FFC (P < 0.000) and LTC (P < 0.000) alignment were significantly different (Table 5). The PSG group subdivided into cut- and pin PSG showed significant difference regarding the mean FFC (P < 0.022) and the LTC (P < 0.009) alignment (Table 6).

DISCUSSION

This industry driven technology proved to be safe, reproducible and easy to use. This leads to a commercial success compared to other computer-assisted technologies^[11]. Although, published results on PSG are contrasted, even on level I studies. Seven level I studies compared conventional instrumentation with PSG and compared different PSG manufacturers. None of them had measured a significant difference in outliers of HKA axis (Table 7). However, Pfitzner *et al*^[24], recently published results comparing conventional instrumentation with CT and MRI based PSG from 2 different manufacturers, and between both PSG groups. They found a significant difference regarding the outliers in HKA-axis between MRI based PSG (Visionaire; 7%) and conventional instruments (43%), but no significant difference between

Table 5 Mean (SD) values and amount of patients and percentages of outliers of > 3° deviation of the planned alignment and postoperative alignment compared between the patient specific matched guides groups, n (%)

	Trumatch	Visionaire	PSI	Signature	P value
HKA outliers	3 (20.00)	1 (7.69)	2 (14.28)	1 (6.66)	0.819
Mean (SD)	178.5 (2.3)	181.3 (1.6)	180.6 (1.6)	177.9 (1.8)	0.000
FFC outliers	0	0	0	0	1.000
Mean (SD)	89.9 (1.6)	90.1 (1.5)	89.9 (1.2)	87.9 (1.8)	0.000
FTC outliers	0	0	1 (7.14)	0	1.000
Mean (SD)	89.3 (1.4)	90.0 (1.2)	89.9 (1.6)	90.6 (1.3)	0.081
LFC outliers	2 (13.33)	2 (15.38)	1 (7.14)	4 (26.66)	0.663
Mean (SD)	85.7 (1.6)	85.4 (2.1)	87.4 (1.9)	85.8 (4.5)	0.307
LTC outliers	2 (13.33)	4 (30.76)	2 (14.28)	1 (6.66)	0.594
Mean (SD)	92.7 (2.4)	91.2 (3.0)	94.8 (1.2)	92.8 (2.7)	0.000

PSI: Patient-specific instrument; HKA: Hip-knee-ankle angle; FFC: Frontal femoral component; FTC: Frontal tibial component; LFC: Flexion/extension of the femur component; LTC: Lateral tibial component.

Table 6 Mean (SD) values and amount of patients and percentages of outliers of > 3° deviation of the planned alignment and postoperative alignment compared between the cut (n = 28, Trumatch and Visionaire) and pin (n = 29, patient-specific instrument and signature) patient specific matched guides group, n (%)

	Cut PSG	Pin PSG	P value
HKA outliers	4 (14.3)	3 (10.3)	1.000
Mean (SD)	179.9 (2.4)	179.3 (2.2)	0.342
FFC outliers	0	0	1.000
Mean (SD)	90.0 (1.5)	89.6 (1.8)	0.022
FTC outliers	0	1 (3.4)	1.000
Mean (SD)	89.6 (1.3)	90.2 (1.5)	0.115
LFC outliers	4 (14.3)	5 (17.2)	1.000
Mean (SD)	85.6 (1.8)	86.6 (3.5)	0.184
LTC outliers	6 (21.4)	3 (10.3)	0.477
Mean (SD)	92.0 (2.7)	93.8 (2.3)	0.009

PSG: Patient specific matched guides; HKA: Hip-knee-ankle angle; FFC: Frontal femoral component; FTC: Frontal tibial component; LFC: Flexion/extension of the femur component; LTC: Lateral tibial component.

CT based PSG and conventional instruments, neither between both PSG systems^[24]. This was contrary to what Victor *et al*^[25] found. They compared 4 different PSG systems with the conventional technique, operated by 4 surgeons, with more significant outliers for the FTC and LTC in favour of the intra- and extramedular technique (Table 7). Even between the 4 different PSG systems, percentages of outliers of > 3° deviation of the planned HKA and LFC angle were significantly different, ranging from 6% to 45% and 20% to 82%, respectively^[25] (Table 7). Published level I percentages of outliers in the frontal and lateral plane for individual components for both femur and tibia vary and are inconclusive. Outliers of the FFC for the PSG are comparable or less than the conventional intramedular technique. Only 2 authors published significant differences in favour of the MRI based PSG^[17,24]. This was in contrast to the FTC (Table 7). Most of the outcomes are comparable, however, 2 articles published significant better outcome

with extramedular rods^[25,26]. Only Ng *et al*^[22] found significant better outcome with MRI based PSG for the tibia. Level I results are very remarkable in regard to the LTC. These were significantly better with PSG than with conventional instrumentation (Table 7). Most notable are the significant differences that have been found with CT based PSG, which scored poorer outcome regarding to LTC outliers, ranging from 21% to 65%^[19,25-27] (Table 7). A possible explanation for these outcomes can be the limitations in visualization and outlining of intra-articular cartilage in CT based 3D models^[28-31]. Another explanation, based on our experience, is that CT based guides were more difficult to place on the bony surface compared to MRI based guides. Nevertheless, we did not reveal a significant difference between the MRI and CT PSG surgeries for HKA-axis and individual components for the different planes.

There may be some concerns regarding our radiological measurements. A wide variety of different analyses in the literature are used to objectively determine the postoperative position for both the femur and tibia implants (Table 7). Despite a good ICC for the evaluation of the frontal and lateral position of both femur and tibia implants, rotational alignment was not examined. Most of the literature use long-standing radiographs, except for 1 paper which used scout CT scan^[17] and two used full-leg CT scans^[22,27]. Postoperative evaluation on 3D-CT have shown to be a valuable tool to measure position and orientation of both the femur and tibia components and it is more accurate with significantly better femoral rotation alignment after use of PSG^[18,22,32]. Unfortunately, a postoperative 3D-CT is not routinely performed in our clinic. On the other hand, plane radiographs are generally applicable for everyone.

This single surgeon experience with different PSG manufacturers could raise questions about the general applicability. We had the opportunity to use different types of PSG and implants. Based on the experience with TKA, the use of PSG and a possible learning curve, implementation of a new implant system may be a

Table 7 Published level I studies with significant percentage of outliers of > 3° deviation between the patient specific matched guides and conventional intramedular and/or extramedular alignment method for hip-knee-ankle angle axis, frontal femoral component, frontal tibial component, flexion/extension of the femur component, lateral tibial component and axial rotation of the femur and/or tibia component controlled with postoperative X-ray (long-leg standing and/or lateral X-rays) and/or computed tomography

Outliers (%) > 3° deviation	PSG system	Modality	Conventional femur/tibia	Control	Sample size (PSG/conventional)	Significant outliers (%) (PSG/conventional)
Boonen <i>et al</i> ^[16]	Signature	MRI	Intra	X-ray	90/90	LFC (49/65) ¹
Chareancholvanich <i>et al</i> ^[17]	PSI	MRI	Intra/Extra	X-ray and CT	40/40	FFC (0/18) ¹
Chotanaphuti <i>et al</i> ^[18]	TruMatch	CT	Intra/Extra	X-ray and CT	40/40	NA
Hamilton <i>et al</i> ^[19]	TruMatch	Scout CT	Intra/Extra	X-ray	26/26	LTC (65/50) ²
Ng <i>et al</i> ^[22] [Outliers (%) > 2° deviation]	PSI	MRI	Intra	CT	51/27	FTC (27/67) ² , Femoral rotation (16/67) ² , Tibial rotation (22/95) ²
Pfitzner <i>et al</i> ^[24]	TruMatch Visionaire	CT MRI + X-ray	Intra/Extra	X-ray and CT	(30/30)/30	HKA (30/7/43) ² FTC (13/3/23) ¹ Femoral rotation (1/13 /50) ¹
Victor <i>et al</i> ^[25]	Signature TruMatch Visionaire PSI	MRI, CT MRI + X-ray MRI	Intra/Extra	X-ray and CT	(16/16/16/16)/64	FTC (15/3) ¹ LTC (21/3) ² HKA (6/25/45/19) ^{1,3} LFC (62/20/20/56) ^{2,5}
Kotela <i>et al</i> ^[26]	Signature	CT	Intra/Extra	X-ray	49/46	FTC (39/20) ¹
Woolson <i>et al</i> ^[27]	TruMatch	CT	Intra/Extra	CT	22/26	LTC (32/8) ¹
Current study	Signature TruMatch Visionaire PSI	MRI CT MRI + X-ray MRI	Intra	X-ray	(15/13/14/15)/60	FFC (022) ² LFC (16/67) ² LTC (16/42) ¹

¹Statistically significant different, $P \leq 0.05$; ²Statistically significant different, $P \leq 0.005$; ³Outliers > 3° deviation between the different PSG groups. NA: Not applicable for outliers; PSG: Patient specific matched guides; PSI: Patient-specific instrument; CT: Computed tomography; MRI: Magnetic resonance imaging; Intra: Intramedular; Extra: Extramedular; HKA: Hip-knee-ankle angle; FFC: Frontal femoral component; FTC: Frontal tibial component; LFC: Flexion/extension of the femur component; LTC: Lateral tibial component.

potential bias in the outcome^[25]. However, research is mostly performed by high-volume surgeons who probably easier adapt to a new surgical technique than low-volume surgeons or residents. PSG could be an added value in less experienced surgeons due to their simplicity^[19]. On the other hand, we evaluated cut and pin PSG from different manufacturers with less outliers compared to the conventional group.

Our primary goal was to investigate the accuracy of alignment between conventional and PSG and between different PSG systems compared with published level I evidence. A comparison on perioperative and clinical outcome were not made, although there is a trend towards significant shorter operating time^[16-18] and blood loss^[16] with surgeries performed with PSG. However, published results on component sizing are inconclusive to come up with a statement^[18,19,27].

Finally, even though this study was a consecutive series compared with a historical cohort and not a randomized trial, a potential criticism was the sample size and power of this study.

The present study illustrates that this simplified surgical technique for TKA is safe and effective with acceptable radiological outcome. The PSG group shows significantly less outliers compared to the conventional technique. Whether these differences are clinically relevant is questionable and should be investigated on the long term. Based on these single surgeon results, we conclude that PSG are ready for prime time.

ACKNOWLEDGMENTS

The authors want to thank Stef van Hoef for his work in measuring the alignment on digital long-leg standing and lateral radiographs. We also thank Dr. Rob Sollie from Flinders Medical Centre Adelaide, Australia, who served as external reader, and for his comments that greatly improved the manuscript.

COMMENTS

Background

Patients with knee osteoarthritis often results in debilitating function of the knee joint warranting a total knee arthroplasty (TKA). This study aims to present the radiological results of TKA with use of patient specific matched guides (PSG) from different manufacturer in patients suffering from severe osteoarthritis of the knee joint.

Research frontiers

Patients suffering from osteoarthritis of the knee joint can be operated with use of PSG for TKA from different manufacturer. TKA with PSG has concerns regarding accurate implant alignment and the long term survival of the TKA compared to the conventional instrumentation.

Innovations and breakthroughs

In this study, PSG for TKA from different manufacturer restored good biomechanical axis and individual implant alignment in patients suffering from moderate to severe osteoarthritis of the knee joint compared to conventional alignment.

Applications

To summarize, PSG from different manufacturer can be an added value in daily

TKA practice in patients suffering from moderate to severe osteoarthritis of the knee joint compared to the conventional instrumentation for TKA.

Peer-review

The authors compared the accuracy of TKA using patient-specific instruments (PSIs) with that of TKA using the conventional technique. In addition, they compared the accuracy of 4 different manufactured PSI TKAs. In conclusion, TKA using PSIs was more accurate than TKA using the conventional method, and no difference in accuracy was found between the 4 different manufactured PSI TKAs. Regarding the PSI TKA that was recently developed, more research studies, including precision, cost, operation time, blood loss, radiation exposure, and long-term survival, should be conducted in order to examine if it confers more benefits to patients than the conventional TKA. The manuscript could add new information on PSI TKA regarding its accuracy.

REFERENCES

- Bargren JH**, Blaha JD, Freeman MA. Alignment in total knee arthroplasty. Correlated biomechanical and clinical observations. *Clin Orthop Relat Res* 1983; **(173)**: 178-183 [PMID: 6825330]
- Jeffery RS**, Morris RW, Denham RA. Coronal alignment after total knee replacement. *J Bone Joint Surg Br* 1991; **73**: 709-714 [PMID: 1894655]
- Lotke PA**, Ecker ML. Influence of positioning of prosthesis in total knee replacement. *J Bone Joint Surg Am* 1977; **59**: 77-79 [PMID: 833180]
- Ritter MA**, Faris PM, Keating EM, Meding JB. Postoperative alignment of total knee replacement. Its effect on survival. *Clin Orthop Relat Res* 1994; **(299)**: 153-156 [PMID: 8119010 DOI: 10.1097/00003086-199402000-00021]
- Bauwens K**, Matthes G, Wich M, Gebhard F, Hanson B, Ekkernkamp A, Stengel D. Navigated total knee replacement. A meta-analysis. *J Bone Joint Surg Am* 2007; **89**: 261-269 [PMID: 17272438 DOI: 10.2106/JBJS.F.00601]
- Haaker RG**, Stockheim M, Kamp M, Proff G, Breitenfelder J, Ottersbach A. Computer-assisted navigation increases precision of component placement in total knee arthroplasty. *Clin Orthop Relat Res* 2005; **(433)**: 152-159 [PMID: 15805951 DOI: 10.1097/01.blo.0000150564.31880.c4]
- Ng VY**, DeClaire JH, Berend KR, Gulick BC, Lombardi AV. Improved accuracy of alignment with patient-specific positioning guides compared with manual instrumentation in TKA. *Clin Orthop Relat Res* 2012; **470**: 99-107 [PMID: 21809150 DOI: 10.1007/s11999-011-1996-6]
- Song EK**, Seon JK, Park SJ, Jung WB, Park HW, Lee GW. Simultaneous bilateral total knee arthroplasty with robotic and conventional techniques: a prospective, randomized study. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 1069-1076 [PMID: 21311869 DOI: 10.1007/s00167-011-1400-9]
- Song EK**, Seon JK, Yim JH, Netravali NA, Bargar WL. Robotic-assisted TKA reduces postoperative alignment outliers and improves gap balance compared to conventional TKA. *Clin Orthop Relat Res* 2013; **471**: 118-126 [PMID: 22669549 DOI: 10.1007/s11999-012-2407-3]
- Beringer DC**, Patel JJ, Bozic KJ. An overview of economic issues in computer-assisted total joint arthroplasty. *Clin Orthop Relat Res* 2007; **463**: 26-30 [PMID: 17960672]
- Thienpont E**, Bellemans J, Delpont H, Van Overschelde P, Stuyts B, Brabants K, Victor J. Patient-specific instruments: industry's innovation with a surgeon's interest. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2227-2233 [PMID: 23942939 DOI: 10.1007/s00167-013-2626-5]
- Krishnan SP**, Dawood A, Richards R, Henckel J, Hart AJ. A review of rapid prototyped surgical guides for patient-specific total knee replacement. *J Bone Joint Surg Br* 2012; **94**: 1457-1461 [PMID: 23109622 DOI: 10.1302/0301-620X.94B11.29350]
- Nam D**, McArthur BA, Cross MB, Pearle AD, Mayman DJ, Haas SB. Patient-specific instrumentation in total knee arthroplasty: a review. *J Knee Surg* 2012; **25**: 213-219 [PMID: 23057140]
- Barrack RL**, Ruh EL, Williams BM, Ford AD, Foreman K, Nunley RM. Patient specific cutting blocks are currently of no proven value. *J Bone Joint Surg Br* 2012; **94**: 95-99 [PMID: 23118393 DOI: 10.1302/0301-620X.94B11.30834]
- Boonen B**, Schotanus MG, Kort NP. Preliminary experience with the patient-specific templating total knee arthroplasty. *Acta Orthop* 2012; **83**: 387-393 [PMID: 22880715 DOI: 10.3109/17453674.2012.711700]
- Boonen B**, Schotanus MG, Kerens B, van der Weegen W, van Drumpt RA, Kort NP. Intra-operative results and radiological outcome of conventional and patient-specific surgery in total knee arthroplasty: a multicentre, randomised controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2206-2212 [PMID: 23928929 DOI: 10.1007/s00167-013-2620-y]
- Chareancholvanich K**, Narkbunnam R, Pornrattanamaneewong C. A prospective randomised controlled study of patient-specific cutting guides compared with conventional instrumentation in total knee replacement. *Bone Joint J* 2013; **95-B**: 354-359 [PMID: 23450020 DOI: 10.1302/0301-620X.95B3.29903]
- Chotanaphuti T**, Wangwittayakul V, Khuangsirikul S, Foojareonyos T. The accuracy of component alignment in custom cutting blocks compared with conventional total knee arthroplasty instrumentation: prospective control trial. *Knee* 2014; **21**: 185-188 [PMID: 23999209 DOI: 10.1016/j.knee.2013.08.003]
- Hamilton WG**, Parks NL, Saxena A. Patient-specific instrumentation does not shorten surgical time: a prospective, randomized trial. *J Arthroplasty* 2013; **28**: 96-100 [PMID: 23910821 DOI: 10.1016/j.arth.2013.04.049]
- Heyse TJ**, Tibesku CO. Improved femoral component rotation in TKA using patient-specific instrumentation. *Knee* 2014; **21**: 268-271 [PMID: 23140905 DOI: 10.1016/j.knee.2012.10.009]
- Koch PP**, Müller D, Pisan M, Fucentese SF. Radiographic accuracy in TKA with a CT-based patient-specific cutting block technique. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2200-2205 [PMID: 23942882 DOI: 10.1007/s00167-013-2625-6]
- Ng VY**, Arnott L, Li J, Hopkins R, Lewis J, Sutphen S, Nicholson L, Reader D, McShane MA. Comparison of custom to standard TKA instrumentation with computed tomography. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 1833-1842 [PMID: 23979518 DOI: 10.1007/s00167-013-2632-7]
- Spencer BA**, Mont MA, McGrath MS, Boyd B, Mitrick MF. Initial experience with custom-fit total knee replacement: intra-operative events and long-leg coronal alignment. *Int Orthop* 2009; **33**: 1571-1575 [PMID: 19099305 DOI: 10.1007/s00264-008-0693-x]
- Pfützner T**, Abdel MP, von Roth P, Perka C, Hommel H. Small improvements in mechanical axis alignment achieved with MRI versus CT-based patient-specific instruments in TKA: a randomized clinical trial. *Clin Orthop Relat Res* 2014; **472**: 2913-2922 [PMID: 25024031 DOI: 10.1007/s11999-014-3784-6]
- Victor J**, Dujardin J, Vandenneucker H, Arnout N, Bellemans J. Patient-specific guides do not improve accuracy in total knee arthroplasty: a prospective randomized controlled trial. *Clin Orthop Relat Res* 2014; **472**: 263-271 [PMID: 23616267 DOI: 10.1007/s11999-013-2997-4]
- Kotela A**, Kotela I. Patient-specific computed tomography based instrumentation in total knee arthroplasty: a prospective randomized controlled study. *Int Orthop* 2014; **38**: 2099-2107 [PMID: 24968788 DOI: 10.1007/s00264-014-2399-6]
- Woolson ST**, Harris AH, Wagner DW, Giori NJ. Component alignment during total knee arthroplasty with use of standard or custom instrumentation: a randomized clinical trial using computed tomography for postoperative alignment measurement. *J Bone Joint Surg Am* 2014; **96**: 366-372 [PMID: 24599197 DOI: 10.2106/JBJS.L.01722]
- Choi JY**, Choi JH, Kim NK, Kim Y, Lee JK, Kim MK, Lee JH, Kim MJ. Analysis of errors in medical rapid prototyping models. *Int J Oral Maxillofac Surg* 2002; **31**: 23-32 [PMID: 11936396 DOI: 10.1054/ijom.2000.0135]
- Duryea J**, Neumann G, Brem MH, Koh W, Noorbakhsh F, Jackson RD, Yu J, Eaton CB, Lang P. Novel fast semi-automated software

- to segment cartilage for knee MR acquisitions. *Osteoarthritis Cartilage* 2007; **15**: 487-492 [PMID: 17188525]
- 30 **Joffe JM**, Nicoll SR, Richards R, Linney AD, Harris M. Validation of computer-assisted manufacture of titanium plates for cranioplasty. *Int J Oral Maxillofac Surg* 1999; **28**: 309-313 [PMID: 10416902 DOI: 10.1016/S0901-5027(99)80165-9]
- 31 **Winder J**, Bibb R. Medical rapid prototyping technologies: state of the art and current limitations for application in oral and maxillofacial surgery. *J Oral Maxillofac Surg* 2005; **63**: 1006-1015 [PMID: 16003630 DOI: 10.1016/j.joms.2005.03.016]
- 32 **Hirschmann MT**, Konala P, Amsler F, Iranpour F, Friederich NF, Cobb JP. The position and orientation of total knee replacement components: a comparison of conventional radiographs, transverse 2D-CT slices and 3D-CT reconstruction. *J Bone Joint Surg Br* 2011; **93**: 629-633 [PMID: 21511928 DOI: 10.1302/0301-620X.93 B5.25893]

P- Reviewer: Anand A, Ohishi T
S- Editor: Song XX **L- Editor:** A **E- Editor:** Li D



Surgical treatment of sacral fractures following lumbosacral arthrodesis: Case report and literature review

Yu Wang, Xian-Yi Liu, Chun-De Li, Xiao-Dong Yi, Zheng-Rong Yu

Yu Wang, Xian-Yi Liu, Chun-De Li, Xiao-Dong Yi, Zheng-Rong Yu, Department of Orthopaedics, Peking University First Hospital, Beijing 100034, China

Author contributions: Wang Y, Li CD and Yi XD designed the research study; Liu XY performed the surgeries; Yu ZR revised the manuscript.

Institutional review board statement: The study was reviewed and approved by the Peking University First Hospital Institutional Review Board.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest concerning this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Xian-Yi Liu, MD, Department of Orthopaedics, Peking University First Hospital, Xishiku Street 8, Xicheng District, Beijing 100034, China. wangyuspine@sina.com
Telephone: +86-10-83575763
Fax: +86-10-66551554

Received: January 2, 2015

Peer-review started: January 2, 2015

First decision: January 20, 2015

Revised: June 28, 2015

Accepted: July 21, 2015

Article in press: July 23, 2015

Published online: January 18, 2016

Abstract

Sacral fractures following posterior lumbosacral fusion are an uncommon complication. Only a few case series and case reports have been published so far. This article presents a case of totally displaced sacral fracture following posterior L4-S1 fusion in a 65-year-old patient with a 15-year history of corticosteroid use who underwent open reduction and internal fixation using iliac screws. The patient was followed for 2 years. A thorough review of the literature was conducted using the Medline database between 1994 and 2014. Immediately after the revision surgery, the patient's pain in the buttock and left leg resolved significantly. The patient was followed for 2 years. The weakness in the left lower extremity improved gradually from 3/5 to 5/5. In conclusion, the incidence of postoperative sacral fractures could have been underestimated, because most of these fractures are not visible on a plain radiograph. Computed tomography has been proved to be able to detect most such fractures and should probably be performed routinely when patients complain of renewed buttock pain within 3 mo after lumbosacral fusion. The majority of the patients responded well to conservative treatments, and extending the fusion construct to the iliac wings using iliac screws may be needed when there is concurrent fracture displacement, sagittal imbalance, neurologic symptoms, or painful nonunion.

Key words: Sacral fracture; Insufficiency fracture; Surgical treatment; Complication; Lumbosacral fusion; Revision surgery

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Sacral fractures following posterior lumbosacral fusion are rare. This article presents a case of totally displaced sacral fracture following posterior L4-S1

fusion. Computed tomography has been proved to be able to detect most such fractures and should probably be performed routinely when patients complain of renewed buttock pain within 3 mo after lumbosacral fusion. The majority of the patients responded well to conservative treatments, and extending the fusion construct to the iliac wings using iliac screws may be needed when there is concurrent fracture displacement, sagittal imbalance, neurologic symptoms, or painful nonunion.

Wang Y, Liu XY, Li CD, Yi XD, Yu ZR. Surgical treatment of sacral fractures following lumbosacral arthrodesis: Case report and literature review. *World J Orthop* 2016; 7(1): 69-73 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i1/69.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i1.69>

INTRODUCTION

Sacral fractures following posterior lumbosacral fusion are an uncommon complication, previously described in only a few case series and case reports. Although these sacral fractures are rarely reported, their incidence could be much higher than previously thought. One of the reasons for underdiagnosis of these fractures is that they are usually unrecognized on plain radiographs, and establishment of a diagnosis is often dependent on computed tomography (CT) or magnetic resonance imaging (MRI). Another reason is that many of these fractures can heal without intervention in a few months, which makes them difficult to be noticed by doctors.

Risk factors for developing sacral fractures following lumbosacral fusions have been identified by several authors. They include old age, female sex, obesity, smoking, postmenopausal osteoporosis, chronic corticosteroid use, prior radiation therapy, graft harvesting, multisegmental lumbosacral fusion, and abnormal spinopelvic alignment. According to the reported experience, most of these fractures occurred within 3 mo after surgery, and the majority of these patients responded well to conservative therapy. Surgical intervention may be needed when there are persistent neurological deficits, significant displacements, severe pain, or fracture nonunion.

This article presents a case of totally displaced sacral fracture following posterior L4-S1 fusion in a 65-year-old patient with a 15-year history of corticosteroid use who underwent open reduction and internal fixation using iliac screws.

CASE REPORT

The current case was a 65-year-old overweight female (body mass index = 25.63 kg/m²) who presented with a chief complaint of 5 years of progressively increased left lower extremity pain and difficulty in walking, which were refractory to conservative management.

The patient was ambulant with 4/5 lower extremity weakness. Both Hoffmann's sign and Babinski's sign were negative. The patient suffered from asthma and had a 15-year history of corticosteroid use. A bone density test of the hip (T-score to -3.7) showed poor bone quality.

Roentgenograms revealed grade 2 anterolisthesis of L5 on S1. The MRI of the spine found central lumbar spinal stenosis at the L5/S1 level and L4-S1 foraminal narrowing (Figure 1). L4-S1 posterior fusion with polyaxial pedicle screws and double rods (XIA II, Stryker) was performed with posterolateral bone grafting using an autologous lamina/spinous process. A cage was also inserted into the L5/S1 disc.

The patient tolerated the procedure well and was walking well on the first postoperative day. On the 5th day after surgery, however, the patient reported a sudden exacerbation of bilateral buttock pain, left-leg radicular pain and sphincter disturbances without precedent trauma. Physical examination revealed a 3/5 weakness of the left lower extremity. A CT scan revealed a horizontal fracture at the S1/S2 level with S2 being totally displaced (Figure 2).

We tried to reduce the fracture with traction but failed. Considering the significant neurological deficits and severe S2 displacement, we performed posterior neural decompression and hardware revision with deformity reduction for the patient at 2 wk after the index operation. The fusion construct was extended to the iliac wings using iliac screws (Figures 3 and 4).

Immediately after the revision surgery, the patient's pain in the buttock and left leg resolved significantly. The patient was followed for 2 years. The weakness of the left lower extremity improved gradually from 3/5 to 5/5.

The sagittal radiographic parameters are listed in Table 1. The preoperative values indicate that she had a high PI (64.1°) and SS (37.1°).

DISCUSSION

Sacral fractures following posterior lumbosacral fusion are rarely seen, and there has been a paucity of data on the association in the published literature. Before 2013, only 34 cases had been reported. No cohort with more than 5 cases had been published until recently. Many spine surgeons have never encountered or noticed such a type of fracture.

Incidence and diagnosis

The incidence of postoperative sacral fractures could have been rather underestimated. Because most of these fractures are not visible on a plain radiograph, diagnosis is mostly established based on CT, MRI, or nuclear scintigraphy. There are 2 studies with a larger cohort that have been published recently. Meredith *et al*^[1] included all patients undergoing posterior lumbosacral arthrodesis at their institution between 2002 and 2011. Twenty-four out of 392 (6.1%) patients

Table 1 The sagittal parameters in the lateral radiographs

	Pelvic incidence	Sacral slope	Pelvic tilt	Lumbar lordosis
Before index surgery	64.1°	37.1°	27°	53.9°
After index surgery	N/A	36.7°	N/A	51.3°
After revision surgery	N/A	30.3°	N/A	47.4°
2 yr	N/A	31.4°	N/A	45.9°

Pelvic incidence is the angle formed by the perpendicular line to the tangent line to the center of the sacral plateau and the line connecting this center of the bicoxofemoral axis. Pelvic tilt is the angle between the vertical plane and the line connecting the center of the sacral plateau and the center of the bicoxofemoral axis. The lumbar lordosis is measured between the cranial endplate of L1 and caudal endplate of L5. N/A: Not applicable because of the displacement of S1.

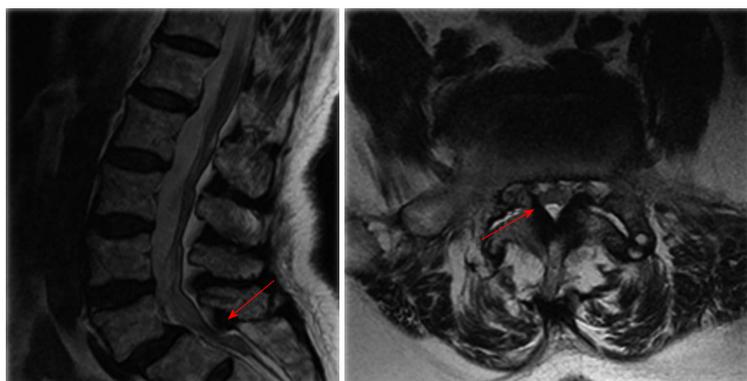


Figure 1 Magnetic resonance imaging of the spine found central lumbar spinal stenosis at L5/S1 level and L4-S1 foraminal narrowing.

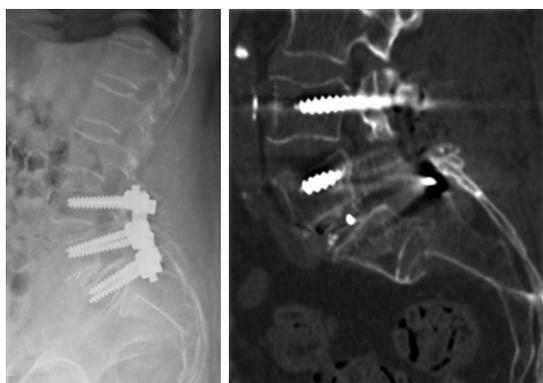


Figure 2 A computed tomography scan revealed a horizontal fracture at the S1/S2 level with S2 being totally displaced.

presented with sacral fractures after surgery, which were confirmed by CT, MRI, or nuclear scintigraphy. However, in only one out of the 24 cases, could the sacral fracture be noticed on the postoperative radiographs. Wilde *et al.*^[2] reported a cohort of 23 patients who had sacral fractures after lumbosacral fusion. Similarly, the sacral fracture was noticed in only one out of 23 patients on the postoperative radiographs. As such, sacral fractures after lumbosacral fusion could have been greatly underdiagnosed. CT has proven to be able to detect most of such fractures and should probably be performed routinely when patients complain of renewed buttock pain within 3 mo after lumbosacral fusion.

Risk factors and prevention

Old age, female sex, osteoporosis, obesity, and a long moment arm of multisegmental lumbosacral fusion are the most frequently cited risk factors for sacral fractures after posterior lumbosacral fusion. The current case had a 15-year history of corticosteroid use for her asthma. The bone density test of the hip (T-score to -3.7) showed a poor bone quality. Furthermore, abnormal spinopelvic alignment could also be a risk factor for fracture development.

To prevent the onset of postoperative sacral fractures, fixation of the iliac wings can be considered in high-risk patients.

Surgical treatment

The reported experience showed us that these postoperative sacral fractures responded well to conservative treatments, which included activity modification, external immobilization, and medical treatment of osteoporosis^[3-5]. However, sacral insufficiency fractures with significant displacement, sagittal imbalance, neurologic symptoms, or painful nonunion may necessitate surgical stabilization. The most commonly performed procedure is to extend the fusion construct to the iliac wings using iliac screws. Fracture union and pain relief were achieved in all the surgically treated cases reported in the literature^[1-8].

In conclusion, the incidence of postoperative sacral fractures could have been rather underestimated, because most of these fractures are not visible on a

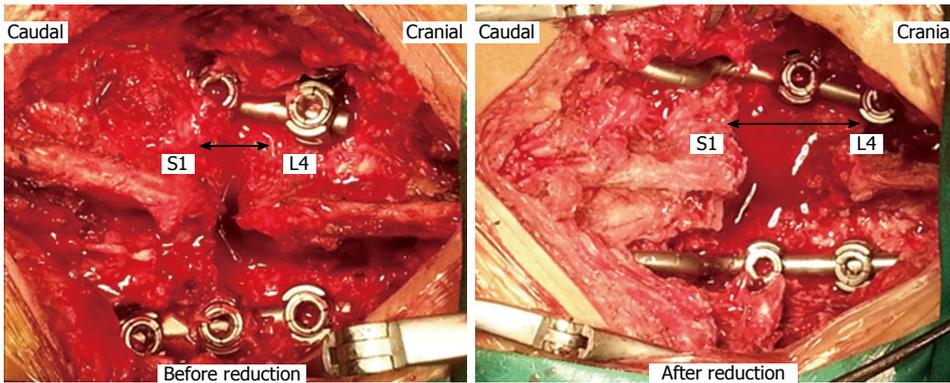


Figure 3 The interspinous process of the sacrum was totally displaced. It moved backward and cranially onto the back of the instruments. To reduce the fracture, we used a spreader to distract the spinal processes of S1 and L4, which was effective. After the distraction, the distance between the spinal processes of the S1 and L4 increased significantly.



Figure 4 Sacral fracture found on the 5th day after surgery. Two weeks after the index operation, the fusion construct was extended to the iliac wings using iliac screws.

plain radiograph. CT has been proved to be able to detect most of such fractures and should probably be performed routinely when patients complain of renewed buttock pain within 3 mo after lumbosacral fusion. The majority of the patients responded well to conservative treatments, and extending the fusion construct to the iliac wings using iliac screws may be needed when there is concurrent fracture displacement, sagittal imbalance, neurologic symptoms, or painful nonunion.

COMMENTS

Case characteristics

A 65-year-old patient with a 15-year history of corticosteroid use reported a sudden exacerbation of bilateral buttock pain, left-leg radicular pain and sphincter disturbances without precedent trauma on the 5th day after posterior L4-S1 fusion.

Clinical diagnosis

Physical examination revealed a 3/5 weakness of left lower extremity.

Differential diagnosis

Osteoporotic vertebral compressive fracture, epidural hematoma, malposition of pedicle screws, and migration of pedicle screws.

Imaging diagnosis

A computed tomography (CT) scan revealed a horizontal fracture at the S1/S2 level with S2 being totally displaced.

Treatment

The authors performed posterior neural decompression and hardware revision with deformity reduction for the patient at 2 wk after the index operation. The fusion construct was extended to the iliac wings using iliac screws.

Related reports

Sacral fractures following posterior lumbosacral fusion are rarely seen, there has been a paucity of data on the association of this condition in the published literature. Before 2013, there were only 34 cases that had been reported. No cohort with more than 5 cases had been published until recently.

Term explanation

Sacral fractures following posterior lumbosacral fusion are an uncommon complication. Risk factors include old age, female sex, obesity, smoking, postmenopausal osteoporosis, chronic corticosteroid use, prior radiation therapy, graft harvesting, multisegmental lumbosacral fusion, and abnormal spinopelvic alignment.

Experiences and lessons

The incidence of postoperative sacral fractures could have been rather underestimated, because most of these fractures are not visible on plain

radiograph. CT has been proved to be able to detect most of such fractures and should probably be performed routinely when patients complain of renewed buttock pain within 3 mo after lumbosacral fusion. The majority of the patients responded well to conservative treatments, and extending the fusion construct to the iliac wings using iliac screws may be needed when there is concurrent fracture displacement, sagittal imbalance, neurologic symptoms, or painful nonunion.

Peer-review

It's a well-organised study.

REFERENCES

- 1 **Meredith DS**, Taher F, Cammisa FP, Girardi FP. Incidence, diagnosis, and management of sacral fractures following multilevel spinal arthrodesis. *Spine J* 2013; **13**: 1464-1469 [PMID: 23623635 DOI: 10.1016/j.spinee.2013.03.025]
- 2 **Wilde GE**, Miller TT, Schneider R, Girardi FP. Sacral fractures after lumbosacral fusion: a characteristic fracture pattern. *AJR Am J Roentgenol* 2011; **197**: 184-188 [PMID: 21701029 DOI: 10.2214/AJR.10.5902]
- 3 **Mathews V**, McCance SE, O'Leary PF. Early fracture of the sacrum or pelvis: an unusual complication after multilevel instrumented lumbosacral fusion. *Spine (Phila Pa 1976)* 2001; **26**: E571-E575 [PMID: 11740374 DOI: 10.1097/00007632-200112150-00027]
- 4 **Fourney DR**, Prabhu SS, Cohen ZR, Gokaslan ZL, Rhines LD. Early sacral stress fracture after reduction of spondylolisthesis and lumbosacral fixation: case report. *Neurosurgery* 2002; **51**: 1507-1510; discussion 1510-1511 [PMID: 12445359]
- 5 **Elias WJ**, Shaffrey ME, Whitehill R. Sacral stress fracture following lumbosacral arthrodesis. Case illustration. *J Neurosurg* 2002; **96**: 135 [PMID: 11795703]
- 6 **Wood KB**, Schendel MJ, Ogilvie JW, Braun J, Major MC, Malcom JR. Effect of sacral and iliac instrumentation on strains in the pelvis. A biomechanical study. *Spine (Phila Pa 1976)* 1996; **21**: 1185-1191 [PMID: 8727193 DOI: 10.1097/00007632-199605150-00010]
- 7 **Gotis-Graham I**, McGuigan L, Diamond T, Portek I, Quinn R, Sturgess A, Tulloch R. Sacral insufficiency fractures in the elderly. *J Bone Joint Surg Br* 1994; **76**: 882-886 [PMID: 7983111]
- 8 **Odate S**, Shikata J, Kimura H, Soeda T. Sacral fracture after instrumented lumbosacral fusion: analysis of risk factors from spinopelvic parameters. *Spine (Phila Pa 1976)* 2013; **38**: E223-E229 [PMID: 23169071 DOI: 10.1097/BRS.0b013e31827dc000]

P- Reviewer: Emara K, Erkan S

S- Editor: Gong XM **L- Editor:** Cant MR **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 February 18; 7(2): 74-148



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

Contents

Monthly Volume 7 Number 2 February 18, 2016

EDITORIAL

- 74 Bone and high-density lipoprotein: The beginning of a beautiful friendship
Papachristou DJ, Blair HC
- 78 Controversies in management of slipped capital femoral epiphysis
Johari AN, Pandey RA

REVIEW

- 82 Biomechanics of the anterior cruciate ligament: Physiology, rupture and reconstruction techniques
Domnick C, Raschke MJ, Herbort M

MINIREVIEWS

- 94 Direct anterior total hip arthroplasty: Comparative outcomes and contemporary results
Connolly KP, Kamath AF
- 102 Osteochondritis dissecans of the capitellum in adolescents
van Bergen CJA, van den Ende KIM, ten Brinke B, Eygendaal D
- 109 Tumors of the spine
Cifdemir M, Kaya M, Selcuk E, Yalniz E

ORIGINAL ARTICLE

Basic Study

- 117 Effect of elbow position on radiographic measurements of radio-capitellar alignment
Sandman E, Canet F, Petit Y, Laflamme GY, Athwal GS, Rouleau DM

Prospective Study

- 123 Reverse-total shoulder arthroplasty cost-effectiveness: A quality-adjusted life years comparison with total hip arthroplasty
Bachman D, Nyland J, Krupp R

SYSTEMATIC REVIEWS

- 128 Corrective osteotomies of the radius: Grafting or not?
Mugnai R, Tarallo L, Lancellotti E, Zambianchi F, Di Giovine E, Catani F, Adani R
- 136 Photogrammetry as a tool for the postural evaluation of the spine: A systematic review
Furlanetto TS, Sedrez JA, Candotti CT, Loss JF

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Dr. Hammad Malik, FRSC, Lecturer, School of Medicine, the University of Manchester, Manchester M20 2EU, United Kingdom

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthritis, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Su-Qing Liu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLICATION DATE
 February 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjgnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>

Bone and high-density lipoprotein: The beginning of a beautiful friendship

Dionysios J Papachristou, Harry C Blair

Dionysios J Papachristou, Department of Anatomy-Histology-Embryology, Unit of Bone and Soft Tissue Studies, University of Patras, School of Medicine, 26504 Rion-Patras, Greece

Dionysios J Papachristou, Harry C Blair, Department of Pathology, University of Pittsburgh, Pittsburgh, PA 15261, United States

Harry C Blair, Pittsburgh VA Medical Center, Pittsburgh, PA 15261, United States

Author contributions: Papachristou DJ conceived the general idea of the paper; Papachristou DJ and Blair HC wrote the paper.

Conflict-of-interest statement: The authors declare no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dionysios J Papachristou, MD, PhD, Consultant Histopathologist, Associate Professor, Department of Anatomy-Histology-Embryology, Unit of Bone and Soft Tissue Studies, University of Patras, School of Medicine, University Campus, Building of Preclinical Studies, 2nd Floor, Room B48, 26504 Rion-Patras, Greece. papachristoudj@med.upatras.gr
Telephone: +30-2610-969188
Fax: +30-2610-969178

Received: July 5, 2015

Peer-review started: July 13, 2015

First decision: September 22, 2015

Revised: November 7, 2015

Accepted: December 1, 2015

Article in press: December 2, 2015

Published online: February 18, 2016

Abstract

There is a tight link between bone and lipid metabolic pathways. In this vein, several studies focused on the exploration of high-density lipoprotein (HDL) in the pathobiology of bone diseases, with emphasis to the osteoarthritis (OA) and osteoporosis, the most common bone pathologies. Indeed, epidemiological and *in vitro* data have connected reduced HDL levels or dysfunctional HDL with cartilage destruction and OA development. Recent studies uncovered functional links between HDL and OA fueling the interesting hypothesis that OA could be a chronic element of the metabolic syndrome. Other studies have linked HDL to bone mineral density. Even though at epidemiological levels the results are conflicting, studies in animals as well as *in vitro* experiments have shown that HDL facilitates osteoblastogenesis and bone synthesis and most probably affects osteoclastogenesis and osteoclast bone resorption. Notably, reduced HDL levels result in increased bone marrow adiposity affecting bone cells function. Unveiling the mechanisms that connect HDL and bone/cartilage homeostasis may contribute to the design of novel therapeutic agents for the improvement of bone and cartilage quality and thus for the treatment of related pathological conditions.

Key words: High-density lipoprotein; Cartilage; Bone; Osteoarthritis; Osteoporosis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Recent evidence suggests that high-density lipoprotein (HDL) metabolic pathways are closely related to bone and cartilage homeostasis. In this editorial the authors briefly present the current knowledge concerning the mechanisms that link HDL and cartilage and bone metabolism and discuss the role of HDL result in the development of the most common bone

pathological conditions, osteoarthritis and osteoporosis. These data add to the appreciation of bone and lipid connection and pave the way towards the development of novel HDL-related strategies for the treatment of these diseases.

Papachristou DJ, Blair HC. Bone and high-density lipoprotein: The beginning of a beautiful friendship. *World J Orthop* 2016; 7(2): 74-77 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/74.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.74>

It is now accepted that there is a strong connection between lipid metabolism and bone-cartilage homeostasis^[1,2]. Indeed, it has been shown that lipid metabolic pathways differentially affect bone cells, leading to the development of pathological bone conditions, *via* both systemic and local phenomena. However, the molecular mechanisms that underline the bone-lipid connection have not been fully illuminated yet. The past few years several, epidemiological studies and studies on animal models focus on the implication of high density lipoprotein (HDL) in the development of bone-related diseases with emphasis to the most common bone pathologies, osteoarthritis (OA) and osteoporosis (OP).

HDL is a vital constituent of the lipoprotein transport system, regulating plasma and tissue lipid metabolism and homeostasis. Apolipoprotein A1 (ApoA1), the lipid transporter ATP-binding-cassette transporter A1 (ABCA1) and the plasma enzyme LCAT are required for the biosynthesis and maturation of HDL. Plasma ApoA-1 is a 243-residue protein, which synthesis takes place primarily in the liver and intestine. ApoA-1 is one of the major apolipoproteins of HDL, since it is responsible for the formation of discoidal HDL particles that mature and become spherical by the action of LCAT^[3,4]. LCAT is synthesized and then secreted primarily by the liver catalyzing the esterification of free cholesterol of lipoproteins by transferring a fatty-acyl group from the C-2 position of lecithin to the 3-hydroxyl group of cholesterol. ApoA1 facilitates LCAT activation in plasma^[4].

Several lines of evidence associate reduced HDL levels with the development of OA. Indeed, it is now well received that OA is strongly connected to cardiovascular and metabolic pathologies namely hypertension hypercholesterolemia, diabetes type 2, which in turn are associated to altered fat metabolism^[5]. Further to support this notion, recent epidemiological data propose that patients with OA have significantly reduced HDL levels compared to healthy individuals. Regrettably, however, the molecular mechanisms that link HDL to cartilage degeneration are still vague. A recent research work has shown that the OA patients have greatly reduced expression of ApoA1 in hyaline or articular cartilage, suggesting that ApoA1-dependent HDL reduction affects

hyaline cartilage homeostasis^[6]. In addition, a very interesting *in vitro* study that used cartilage and synovial membrane joint cells from patients with OA having undergone joint replacement therapy, showed that ApoA1 has the ability to induce the expression of interleukin-6 (IL-6), mouse matrix metalloproteinase-1 (MMP-1) and MMP-3 by primary chondrocytes and fibroblast-like synoviocytes *via* the toll-like receptor 4 receptor. The authors proposed that the lipid metabolic profile is deregulated in the synovial fluid of OA patients and that apoA-1 exhibits pro-inflammatory properties responsible for the symptoms associated with OA^[7]. Aiming at further investigating the HDL-OA connection, Collins-Racie *et al*^[6], showed that LXR signaling is implicated in the pathobiology of OA. The liver X receptors (LXR α /NR1H3 and LXR β /NR1H2) are oxysterol-activated transcription factors of the nuclear receptor family that regulate the homeostasis of cholesterol at both cellular and whole-body level and have robust anti-inflammatory functions. They also demonstrated that the expression levels of LXR α and β , as well as the expression levels of the LXR target genes ABCG1 and apolipoproteins D and E were altered, a finding implying that the LXR signaling cascade is dysfunctional in degenerated OA cartilage. Importantly, they propose that use of LXR signaling modulators as therapeutic alternative to standard joint glucocorticoid injections^[6]. In the same vein Tsezou *et al*^[8], studied the expression of genes that regulate cholesterol efflux in human OA chondrocytes. In harmony with previous reports having demonstrated that distorted lipid metabolism is critically involved in OA they demonstrated that the expression of ABCA1, ApoA1, and LXR α and LXR β genes that control cholesterol efflux is greatly reduced in OA compared to normal chondrocytes. Moreover they showed that treatment of osteoarthritic chondrocytes with the LXR agonist TO-901317 resulted in the enhancement of the ApoA1 and ABCA1 expression and cholesterol efflux^[8].

In our further effort to explore the involvement of HDL-related metabolic pathways in the pathogenesis of OA we examined the effect of HDL deficiency and impaired maturation on OA development using ApoA1 and LCAT knock out, as well as wild-type mice. Both animal groups were fed both chow (standard) and Western-type (high-fat) diet. Our findings were intriguing. Indeed, we found that the LCAT^{-/-} mice developed marked diet-induced obesity in comparison to the C57BL/6 and ApoA1^{-/-} groups that were fed Western-type diet. Notably, both the LCAT and the ApoA1 knockout mice developed OA, even though the latter were not obese. These novel findings raise the challenging possibility that alterations in HDL rather than increased mechanical stimulation due to excess body weight most probably result in the development of OA in mice. Moreover, histomorphometrical analysis revealed that the bone marrow from LCAT^{-/-} and ApoA1^{-/-} mice contained remarkably enhanced number of fat cells, compared to the other groups adding to the prevailing notion that bone marrow fat is functionally involved in

the pathobiology of cartilage destruction, most plausibly *via* the production and secretion of adipokines, such as leptin, adiponectin and resistin^[8]. Definitely, the role of HDL metabolic pathways in the development of OA warrants further investigation; however, the vast majority of the existing research data point towards a protective role of HDL against diet-induced OA and suggest that OA probably represents another facet of the metabolic syndrome^[5,9].

Recent data suggest that serum HDL levels and bone mass are connected. Nevertheless, whether this association is positive or negative, is not clear. Indeed, in a relative recent review article on human subjects Ackert-Bicknell very nicely describe a large number of epidemiological studies exploring the link between HDL and bone mineral density. He proposed that the inconsistent results that were presented are attributed to a number of parameters including age, dietary habits, sex, endocrine status and genetic background^[10]. It seems that the research data are clearer in molecular, *in vitro* and animal model studies. Indeed, studies in mice have shown that specific genes such as *APOE*, *PPAR γ* , *ESR1*, *IL-6* that regulate both BMD and HDL exhibit chromosomal co-localization^[10]. In addition, studies on transgenic mice uncovered specific genes that regulate both BMD and HDL serum levels. One of these genes is apolipoprotein E (apoE) that is involved in HDL metabolic pathways. The role of apoE in bone regulation is very intriguing. Indeed, a few years ago an animal model study showed that apoE deficiency is associated with increased bone mass and elevated osteoblastic function, whereas bone resorption is not affected^[11]. Interestingly, however, a few years later the same group showed that when stressed with diabetogenic high-fat diet, the apoE deficient mice develop decreased bone mass and lower body weight^[12]. In addition, these animals display lower serum glucose, insulin and leptin levels compared to the control group. Less is known about the role of apoE in osteoclast function. A recent *in vitro* study unveiled that apoE halts osteoclast differentiation and proposed that this effect is possibly mediated through the inhibition of the RANL-dependent nuclear factor κ B activation and the c-Fos and NFATc1 induction^[13]. Genetic analyses in mice also demonstrated that human apoE isoforms have different effects on bone mass and bone turnover. More specifically, Kim *et al.*^[14], showed that human apoE2 strongly influences trabecular (but not cortical) bone metabolism in knock-in mice and highlighted the possibility that apoE ϵ 2 allele might serve as a genetic risk factor vertebral fractures in humans^[15].

Scavenger receptor class B type I is the product of *Scarb1* gene, and its major function is the uptake of cholesteryl esters of HDL by the liver and other tissues. The implication of *Scarb1* in bone metabolism has very recently started to be investigated. However, the results generated seem to be very interesting. Using static and dynamic histomorphometric analyses, Martineau *et al.*^[16] showed that *Scarb1* deficiency results in augmented bone mass that was more evident in the trabecular

bones of 2 mo old female mice^[14]. In symphony with the histomorphometry data, *in vitro* assays revealed that the expression levels of the osteoblastic transcription factor *Osx/Sp7* were enhanced, whereas the mRNA levels of the caveolin 1, a gene that halts osteoblastic progenitor differentiation, were reduced. Notably, the number of TRAP-positive surface remained unaffected in these KO mice. In an effort to further explore the role of *Scarb1* in osteoblastogenesis, the same group performed a series of *in vitro* assays on mesenchymal stem cells obtained from *Scarb1* deficient and wild-type mice and concluded that the enhanced osteogenic function that was observed in the *Scarb1* knock-out mice can be attributed to stimulation of the Wnt signaling cascade^[16].

As mentioned previously, studies have shown that HDL deficiency results in the congregation of lipoblasts in the bone marrow of mice. It is also accepted that bone marrow accelerates osteoclastogenesis, while stunts osteoblastogenesis. These data spark the question whether HDL may have an implication in the pathogenesis of other bone pathological conditions, including neoplastic bone diseases. Since bone marrow microenvironment possesses a cardinal role in the development of bone metastasis we are tempted to speculate that HDL may have a protective role towards metastatic bone disease a hypothesis that definitely merits further exploration. In addition, the tight link between bone and fat raises the challenging possibility that the development of drugs that will effectively target lipid-specific metabolic pathways may enhance osteoblast function, improving bone quality.

Collectively, gradually accumulating research evidence suggests that HDL serves as a requirement for normal cartilage and bone function and that it most probably has a protective role against the development of degenerative and metabolic conditions such as OA and OP. Nevertheless, additional epidemiological, molecular, and *in vitro* studies in animal models are needed to substantiate this hypothesis. Furthermore, the role of other molecules that are tightly involved in the HDL metabolic pathways (such as ABCA1), should be carefully examined. Except from HDL-C levels, HDL functionality should also be determined in bone diseases. Indeed, mounting evidence supports the notion that the functionality of HDL particles is plausibly more significant than simply HDL-C levels in plasma and in many instances the anti-inflammatory and antioxidant properties of HDL cannot be evaluated only by the determination of HDL-C plasma levels^[17].

Unfolding the molecular mechanistic events that connect HDL and bone metabolism may pave the way towards the development of HDL-directed therapies that could add to the armamentarium against bone-related diseases.

REFERENCES

- 1 Lecka-Czernik B, Stechschulte LA. Bone and fat: a relationship of different shades. *Arch Biochem Biophys* 2014; **561**: 124-129 [PMID: 24956594 DOI: 10.1016/j.abb.2014.06.010]

- 2 **Tsolis KC**, Bei ES, Papathanasiou I, Kostopoulou F, Gkretsi V, Kalantzaki K, Malizos K, Zervakis M, Tsezou A, Economou A. Comparative proteomic analysis of hypertrophic chondrocytes in osteoarthritis. *Clin Proteomics* 2015; **12**: 12 [PMID: 25945082 DOI: 10.1186/s12014-015-9085-6]
- 3 **Kypreos KE**, Zannis VI. Pathway of biogenesis of apolipoprotein E-containing HDL in vivo with the participation of ABCA1 and LCAT. *Biochem J* 2007; **403**: 359-367 [PMID: 17206937 DOI: 10.1042/BJ20061048]
- 4 **Fisher EA**, Feig JE, Hewing B, Hazen SL, Smith JD. High-density lipoprotein function, dysfunction, and reverse cholesterol transport. *Arterioscler Thromb Vasc Biol* 2012; **32**: 2813-2820 [PMID: 23152494 DOI: 10.1161/ATVBAHA.112.300133]
- 5 **Velasquez MT**, Katz JD. Osteoarthritis: another component of metabolic syndrome? *Metab Syndr Relat Disord* 2010; **8**: 295-305 [PMID: 20367223 DOI: 10.1089/met.2009.0110]
- 6 **Collins-Racie LA**, Yang Z, Arai M, Li N, Majumdar MK, Nagpal S, Mounts WM, Dorner AJ, Morris E, LaVallie ER. Global analysis of nuclear receptor expression and dysregulation in human osteoarthritic articular cartilage: reduced LXR signaling contributes to catabolic metabolism typical of osteoarthritis. *Osteoarthritis Cartilage* 2009; **17**: 832-842 [PMID: 19217805 DOI: 10.1016/j.joca.2008.12.011]
- 7 **de Seny D**, Cobraiville G, Charlier E, Neuville S, Lutteri L, Le Goff C, Malaise D, Malaise O, Chapelle JP, Relic B, Malaise MG. Apolipoprotein-A1 as a damage-associated molecular patterns protein in osteoarthritis: ex vivo and in vitro pro-inflammatory properties. *PLoS One* 2015; **10**: e0122904 [PMID: 25849372 DOI: 10.1371/journal.pone.0122904]
- 8 **Tsezou A**, Iliopoulos D, Malizos KN, Simopoulou T. Impaired expression of genes regulating cholesterol efflux in human osteoarthritic chondrocytes. *J Orthop Res* 2010; **28**: 1033-1039 [PMID: 20108316 DOI: 10.1002/jor.21084]
- 9 **Triantaphyllidou IE**, Kalyvioti E, Karavia E, Lilis I, Kypreos KE, Papachristou DJ. Perturbations in the HDL metabolic pathway predispose to the development of osteoarthritis in mice following long-term exposure to western-type diet. *Osteoarthritis Cartilage* 2013; **21**: 322-330 [PMID: 23151457 DOI: 10.1016/j.joca.2012.11.003]
- 10 **Ackert-Bicknell CL**. HDL cholesterol and bone mineral density: is there a genetic link? *Bone* 2012; **50**: 525-533 [PMID: 21810493 DOI: 10.1016/j.bone.2011.07.002]
- 11 **Schilling AF**, Schinke T, Münch C, Gebauer M, Niemeier A, Priemel M, Streichert T, Rueger JM, Amling M. Increased bone formation in mice lacking apolipoprotein E. *J Bone Miner Res* 2005; **20**: 274-282 [PMID: 15647822 DOI: 10.1359/JBMR.041101]
- 12 **Bartelt A**, Beil FT, Schinke T, Roeser K, Ruether W, Heeren J, Niemeier A. Apolipoprotein E-dependent inverse regulation of vertebral bone and adipose tissue mass in C57Bl/6 mice: modulation by diet-induced obesity. *Bone* 2010; **47**: 736-745 [PMID: 20633710 DOI: 10.1016/j.bone.2010.07.002]
- 13 **Dieckmann M**, Beil FT, Mueller B, Bartelt A, Marshall RP, Koehne T, Amling M, Ruether W, Cooper JA, Humphries SE, Herz J, Niemeier A. Human apolipoprotein E isoforms differentially affect bone mass and turnover in vivo. *J Bone Miner Res* 2013; **28**: 236-245 [PMID: 22991192 DOI: 10.1002/jbmr.1757]
- 14 **Kim WS**, Kim HJ, Lee ZH, Lee Y, Kim HH. Apolipoprotein E inhibits osteoclast differentiation via regulation of c-Fos, NFATc1 and NF-κB. *Exp Cell Res* 2013; **319**: 436-446 [PMID: 23246654 DOI: 10.1016/j.yexcr.2012.12.004]
- 15 **Martineau C**, Kevorkova O, Brissette L, Moreau R. Scavenger receptor class B, type I (Scarb1) deficiency promotes osteoblastogenesis but stunts terminal osteocyte differentiation. *Physiol Rep* 2014; **2**: pii: e12117 [PMID: 25281615 DOI: 10.14814/phy2.12117]
- 16 **Martineau C**, Martin-Falstra L, Brissette L, Moreau R. The atherogenic Scarb1 null mouse model shows a high bone mass phenotype. *Am J Physiol Endocrinol Metab* 2014; **306**: E48-E57 [PMID: 24253048 DOI: 10.1152/ajpendo.00421.2013]
- 17 **Tsompanidi EM**, Brinkmeier MS, Fotiadou EH, Giakoumi SM, Kypreos KE. HDL biogenesis and functions: role of HDL quality and quantity in atherosclerosis. *Atherosclerosis* 2010; **208**: 3-9 [PMID: 19595353 DOI: 10.1016/j.atherosclerosis.2009.05.034]

P- Reviewer: Canavese F, Maheshwari AV, Sakamoto A
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Liu SQ



Controversies in management of slipped capital femoral epiphysis

Ashok N Johari, Ritesh A Pandey

Ashok N Johari, Ritesh A Pandey, Children's Orthopaedic Centre, Mumbai 400016, India

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: No potential conflicts of interest. No financial support.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dr. Ashok N Johari, Director, Children's Orthopaedic Centre, 2nd Floor, Bobby Apartments, 143 L.J. Road, Mahim (West), Mumbai 400016, India. drashokjohari@hotmail.com
Telephone: +91-22-24365050

Received: May 29, 2015

Peer-review started: June 1, 2015

First decision: August 4, 2015

Revised: November 2, 2015

Accepted: November 24, 2015

Article in press: November 25, 2015

Published online: February 18, 2016

Abstract

The traditional treatment of the hip with a slip of the capital femoral epiphysis has been an *in situ* fixation using a single screw. This has the sanctity of a long term result. Recent literature stresses the outcomes of failure to restore the upper femoral alignment and on the basis of the poor results makes a plea for capital realignment.

This being a recent development, it lacks the support of long term follow up and it remains to be seen if this is a better alternative of managing displaced and unstable slipped capital femoral epiphysis. The authors look at some of the available literature on the subject to highlight these controversies and their implications for orthopedic surgeons. Other controversies pertain to contralateral fixation, duration of immobilization and amount of weight bearing after an *in situ* fixation.

Key words: Slipped capital femoral epiphysis; Fixation *in situ*; Femoral head realignment; Osteoplasty; Dunn osteotomy

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This article discusses the current controversies around the treatment of slipped capital femoral epiphysis (SCFE). Newer surgical techniques have brought with them controversies as to the best form of management of different types of SCFE. The authors highlight the current status of management in the light of publications on the above subject.

Johari AN, Pandey RA. Controversies in management of slipped capital femoral epiphysis. *World J Orthop* 2016; 7(2): 78-81 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/78.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.78>

Slipped capital femoral epiphysis (SCFE) is a common condition faced by an orthopaedic surgeon. In 1962, Watson-Jones^[1] lamented that "the treatment of displacement of upper femoral epiphysis is not a very happy chapter in the history of orthopaedic surgery". The litany of complications associated with this condition is long. In recent years, improvements in understanding of the stability status, imaging techniques, and fixation methods

Table 1 Classification of physeal stability

Duration of symptoms	
Acute	Less than 2 wk
Chronic	More than 2 wk
Acute on chronic	Duration of symptoms for more than 2 wk but with sudden deterioration of symptoms
Ability to walk	
Stable	Patient is able to walk
Unstable	Patient is unable to walk

have led to significant changes in this outlook.

Currently, the treatment of SCFE depends on many factors like remaining growth potential of the physis (open or closed), the stability of the slip (stable or unstable), severity of the deformity, presence of femoroacetabular impingement (FAI) and confidence of the surgeon with various surgical options.

Immediate goals of management of an acute SCFE are threefold: (1) pain relief; (2) maintenance of an epiphyseal-femoral neck relationship that will avoid further slip progression; and (3) acceleration of epiphyseodesis so that risk of repeat slippage is eliminated. Long term goals include avoidance of complications that could lead to significant premature secondary degenerative joint disease.

Despite numerous studies and clinical trials, the cause for avascular necrosis (AVN) in SCFE is not very clear. Various hypothesis have been suggested for the cause of AVN; mechanical instability of the physis being one of them. However, the presence of instability at the physis cannot be assessed directly. Two clinical classifications have been suggested (Table 1) to predict the instability at the physis; One depending on the duration of symptoms^[2,3] and the other depending on the patient's walking ability^[4].

In situ fixation with pins or screws is the recommended method of treatment for stable and chronic slips whereas, lots of controversies persist regarding the treatment of unstable or acute cases including the timing of intervention and the method of reduction. Also, physeal stability confirmed by clinical methods did not always matched with intraoperative findings at surgery. Ziebarth *et al*^[5] compared the clinical classifications with the intraoperative findings. Classifying SCFE by the duration of symptoms had a low specificity of 44% and a sensitivity of 82%. Based on the eligibility to walk, the sensitivity was a low 39% and specificity was 76%. Ziebarth *et al*^[5] concluded that the current clinical systems are not accurate to judge physeal stability in SCFE.

In situ central single screw fixation without any attempt for reduction has become the current treatment of choice for stable SCFE^[6]. The surgeons who support this, insist that even though the proximal femoral anatomy is not restored with this treatment, the proximal femur has remodeling potential, especially for patients who are young^[7-9]. Others believe that in unreduced epiphysis FAI leads to mechanical derangement of the hip

and development of secondary osteoarthritis^[10,11]. They believe in restoring the anatomy of the hip joint^[12,13] by a combination of surgical dislocation of hip and a modified Dunn procedure^[10,11]. Ziebarth *et al*^[14] treated forty patients of slipped capital epiphysis with modified Dunn procedure and recommended it as a safe treatment option^[15]. However, up to 17% risk of AVN is reported in all studies of Dunn's osteotomy. Even, addition of surgical dislocation of hip does not decrease the rate of AVN of femoral head as suggested by Alves *et al*^[16] (2012) and Anderson *et al*^[17] (2013). The authors recommend an *in situ* fixation followed by a later osteochondroplasty if felt necessary on a longer follow up.

Even though there is risk of avascular necrosis in unstable slip, reduction in these cases is feasible^[18]. Some recent studies have reported good results of open reduction in unstable slips^[14,19]. On the other hand there have been other reports, notably that of Sankar *et al*^[20] with a 26% osteonecrosis and a 41% overall rate of substantial complications.

Another controversy is the number of screws for fixing the unstable SCFE. Biomechanical studies support the use of two screws as it provides more stable fixation when compared to a single screw. However, most surgeons prefer using a single screw due to the risk of epiphyseal perforation and subsequent chondrolysis with the use of two screws^[21].

Confusion also remains regarding the type of corrective osteotomy (intracapsular/extracapsular) and it's timing for both stable and unstable SCFE^[21]. Although most surgeons accept that cervical osteotomy is a more successful method of gaining anatomical correction, they opt for treatment by subtrochanteric (Southwick *et al*^[21] 1967) or intertrochanteric (Griffiths^[22] 1976) osteotomy because of lower risks of iatrogenic ischemic changes. However these osteotomies fail to restore the abduction power and rotational balance of the hip leading to postoperative Trendelenburg gait. These distal osteotomies also fail to correct the intraarticular incongruity of the hip in cases with a severe slip, leaving the features which lead to early degenerative arthritis. They also create a residual anatomical deformity of the proximal third of femur which may well prejudice any future need for total hip replacement. However, some recent studies report good outcome from these osteotomies^[23].

Cervical osteotomy, by contrast, fulfills the requirements of successful operative treatment, by achieving an anatomical reduction. It therefore reduces the long term risk of osteoarthritis and produces a good postoperative functional result without surgical shortening^[17,24,25].

According to Loder *et al*^[26], there is not enough clinical evidence to prove the superiority of surgical dislocation and osteoplasty over pinning *in situ* for stable SCFEs. They also mention that there is not enough evidence to support the widespread use of surgical dislocation and capital realignment in stable SCFE and suggests further research especially in a large cohort of patients.

Also, there is controversy regarding fixation of contralateral normal hip. The supporters argue for fixation of the opposite hip in all patients in view of high incidence of contralateral slip^[15]. Another group of surgeons recommend fixation of contralateral normal hip only in selective patients due to the risk of possible theoretical complications^[27]. We prefer to avoid unnecessary fixation of the contralateral hip in all cases and suggest fixation of the opposite hip only if risk factors for contralateral slip is present. These are, young age at primary diagnosis, severe slip at primary diagnosis, presence of endocrine disorders like adiposogenital dystrophy, juvenile hypothyroidism and presence of nonspecific obesity. We also fix the contralateral normal hip if patient is on growth hormone therapy. Finally, in those cases where for social and/or geographical reasons the patient is not expected to comply with a protocol of continued regular clinical and radiological observation, prophylactic fixation is considered.

Post-operative protocol is also debated. Controversy remains regarding the timing of bearing weight in stable SCFE. Most of the surgeons prefer to be more careful and delay full weight bearing for several weeks. They recommend longer duration of bed rest and protected weight bearing after surgery. On the other hand, few orthopaedic surgeons recommend a shorter bed rest and allow total weight bearing for mild stable SCFE without any reported complication. This area needs more research to favor early weight bearing this being more comfortable from the patient point of view.

Furthermore, many aspects of treatment are not discussed such as the timing of treatment, (particularly in the management of unstable and severe slipped epiphyses), the use of capsular decompression and implant removal. As these aspects of management do not influence the final outcome significantly, they are not addressed by majority of the orthopedic surgeons. Literature also is unclear about their effect on final outcome and further studies to prove their significance is recommended.

Thus, the management of SCFE remains controversial. There are several areas where knowledge is lacking, and where multi-centric studies could be focused to identify the most effective method of management. Long-term prospective studies, employing both contemporary treatment methods and contemporary outcome measures, are needed to guide improved treatment selection and results for future patients with SCFE.

REFERENCES

- 1 **Watson-Jones R.** The classic: "Fractures and Joint Injuries" by Sir Reginald Watson-Jones, taken from "Fractures and Joint Injuries," by R. Watson-Jones, Vol. II, 4th ed., Baltimore, Williams and Wilkins Company, 1955. *Clin Orthop Relat Res* 1974; **(105)**: 4-10 [PMID: 4609656]
- 2 **Aronsson DD, Loder RT.** Treatment of the unstable (acute) slipped capital femoral epiphysis. *Clin Orthop Relat Res* 1996; **(322)**: 99-110 [PMID: 8542719]
- 3 **Fahey JJ, O'Brien ET.** Acute slipped capital femoral epiphysis:

review of the literature and report of ten cases. *J Bone Joint Surg Am* 1965; **47**: 1105-1127 [PMID: 14337771]

- 4 **Loder RT, Richards BS, Shapiro PS, Reznick LR, Aronson DD.** Acute slipped capital femoral epiphysis: the importance of physeal stability. *J Bone Joint Surg Am* 1993; **75**: 1134-1140 [PMID: 8354671]
- 5 **Ziebarth K, Domayer S, Slongo T, Kim YJ, Ganz R.** Clinical stability of slipped capital femoral epiphysis does not correlate with intraoperative stability. *Clin Orthop Relat Res* 2012; **470**: 2274-2279 [PMID: 22487880]
- 6 **Loder RT, Aronsson DD, Weinstein SL, Breur GJ, Ganz R, Leunig M.** Slipped capital femoral epiphysis. *Instr Course Lect* 2008; **57**: 473-498 [PMID: 18399603 DOI: 10.1201/b13489-77]
- 7 **Bellemans J, Fabry G, Molenaers G, Lammens J, Moens P.** Slipped capital femoral epiphysis: a long-term follow-up, with special emphasis on the capacities for remodeling. *J Pediatr Orthop B* 1996; **5**: 151-157 [PMID: 8866278 DOI: 10.1097/01202412-199605030-00003]
- 8 **Boyer DW, Mickelson MR, Ponseti IV.** Slipped capital femoral epiphysis. Long-term follow-up study of one hundred and twenty-one patients. *J Bone Joint Surg Am* 1981; **63**: 85-95 [PMID: 7451529]
- 9 **Jones JR, Paterson DC, Hillier TM, Foster BK.** Remodelling after pinning for slipped capital femoral epiphysis. *J Bone Joint Surg Br* 1990; **72**: 568-573 [PMID: 2380205]
- 10 **Fraitl CR, Käfer W, Nelitz M, Reichel H.** Radiological evidence of femoroacetabular impingement in mild slipped capital femoral epiphysis: a mean follow-up of 14.4 years after pinning in situ. *J Bone Joint Surg Br* 2007; **89**: 1592-1596 [PMID: 18057358 DOI: 10.1302/0301-620X.89B12.19637]
- 11 **Leunig M, Casillas MM, Hamlet M, Hersche O, Nötzli H, Slongo T, Ganz R.** Slipped capital femoral epiphysis: early mechanical damage to the acetabular cartilage by a prominent femoral metaphysis. *Acta Orthop Scand* 2000; **71**: 370-375 [PMID: 11028885 DOI: 10.1080/00164700317393367]
- 12 **Mamisch TC, Kim YJ, Richolt JA, Millis MB, Kordelle J.** Femoral morphology due to impingement influences the range of motion in slipped capital femoral epiphysis. *Clin Orthop Relat Res* 2009; **467**: 692-698 [PMID: 18941860 DOI: 10.1007/s11999-008-0477-z]
- 13 **Rab GT.** The geometry of slipped capital femoral epiphysis: implications for movement, impingement, and corrective osteotomy. *J Pediatr Orthop* 1999; **19**: 419-424 [PMID: 10412987 DOI: 10.1097/00004694-199907000-00001]
- 14 **Ziebarth K, Zilkens C, Spencer S, Leunig M, Ganz R, Kim YJ.** Capital realignment for moderate and severe SCFE using a modified Dunn procedure. *Clin Orthop Relat Res* 2009; **467**: 704-716 [PMID: 19142692 DOI: 10.1007/s11999-008-0687-4]
- 15 **Hägglund G.** The contralateral hip in slipped capital femoral epiphysis. *J Pediatr Orthop B* 1996; **5**: 158-161 [PMID: 8866279 DOI: 10.1097/01202412-199605030-00004]
- 16 **Alves C, Steele M, Narayanan U, Howard A, Alman B, Wright JG.** Open reduction and internal fixation of unstable slipped capital femoral epiphysis by means of surgical dislocation does not decrease the rate of avascular necrosis: a preliminary study. *J Child Orthop* 2012; **6**: 277-283 [PMID: 23904893 DOI: 10.1007/s11832-012-0423-1]
- 17 **Anderson LA, Gililland JM, Pelt CE, Peters CL.** Subcapital correction osteotomy for malunited slipped capital femoral epiphysis. *J Pediatr Orthop* 2013; **33**: 345-352 [PMID: 23653020 DOI: 10.1097/BPO.0b013e31827d7e06]
- 18 **Lowndes S, Khanna A, Emery D, Sim J, Maffulli N.** Management of unstable slipped upper femoral epiphysis: a meta-analysis. *Br Med Bull* 2009; **90**: 133-146 [PMID: 19376800 DOI: 10.1093/bmb/ldp012]
- 19 **Leunig M, Slongo T, Kleinschmidt M, Ganz R.** Subcapital correction osteotomy in slipped capital femoral epiphysis by means of surgical hip dislocation. *Oper Orthop Traumatol* 2007; **19**: 389-410 [PMID: 17940736]
- 20 **Sankar WN, Vanderhave KL, Matheney T, Herrera-Soto JA, Karlen JW.** The modified Dunn procedure for unstable slipped

- capital femoral epiphysis: a multicenter perspective. *J Bone Joint Surg Am* 2013; **95**: 585-591 [PMID: 23553292 DOI: 10.2106/JBJS.L.00203]
- 21 **Southwick WO**. Osteotomy through the lesser trochanter for slipped capital femoral epiphysis. *J Bone Joint Surg Am* 1967; **49**: 807-835 [PMID: 6029256]
 - 22 **Griffith MJ**. Slipping of the capital femoral epiphysis. *Ann R Coll Surg Engl* 1976; **58**: 34-42 [PMID: 1259324]
 - 23 **Coppola C**, Sadile F, Lotito FM, Cigala F, Shanmugam C, Maffulli N. [Southwick osteotomy in stable slipped capital femoral epiphysis: a long-term outcome study]. *Acta Orthop Traumatol Turc* 2008; **42**: 358-364 [PMID: 19158457 DOI: 10.3944/AOTT.2008.358]
 - 24 **Biring GS**, Hashemi-Nejad A, Catterall A. Outcomes of subcapital cuneiform osteotomy for the treatment of severe slipped capital femoral epiphysis after skeletal maturity. *J Bone Joint Surg Br* 2006; **88**: 1379-1384 [PMID: 17012431]
 - 25 **Slongo T**, Kakaty D, Krause F, Ziebarth K. Treatment of slipped capital femoral epiphysis with a modified Dunn procedure. *J Bone Joint Surg Am* 2010; **92**: 2898-2908 [PMID: 21159990 DOI: 10.2106/JBJS.I.01385]
 - 26 **Loder RT**, Dietz FR. What is the best evidence for the treatment of slipped capital femoral epiphysis? *J Pediatr Orthop* 2012; **32** Suppl 2: S158-S165 [PMID: 22890456 DOI: 10.1097/BPO.0b013e318259f2d1]
 - 27 **Kocher MS**, Bishop JA, Hresko MT, Millis MB, Kim YJ, Kasser JR. Prophylactic pinning of the contralateral hip after unilateral slipped capital femoral epiphysis. *J Bone Joint Surg Am* 2004; **86-A**: 2658-2665 [PMID: 15590850]

P- Reviewer: Anand A, Baldwin K, Martinelli N, Solomon LB

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Liu SQ



Biomechanics of the anterior cruciate ligament: Physiology, rupture and reconstruction techniques

Christoph Domnick, Michael J Raschke, Mirco Herbert

Christoph Domnick, Michael J Raschke, Mirco Herbert, Department of Trauma, Hand and Reconstructive Surgery, Westphalian Wilhelms University Muenster, 48149 Muenster, Germany

Author contributions: Domnick C, Raschke MJ and Herbert M performed the research and wrote the paper.

Supported by A Research Fellowship from the Faculty of Medicine, Westphalian Wilhelms University Muenster to Domnick C.

Conflict-of-interest statement: There are no conflicts of interest to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Mirco Herbert, MD, Privatdozent, Department of Trauma, Hand and Reconstructive Surgery, Westphalian Wilhelms University Muenster, Waldeyer Strasse 1, 48149 Muenster, Germany. mirco.herbert@uni-muenster.de
Telephone: +49-251-8356301
Fax: +49-251-8356318

Received: June 1, 2015

Peer-review started: June 5, 2015

First decision: August 16, 2015

Revised: September 5, 2015

Accepted: December 1, 2015

Article in press: December 2, 2015

Published online: February 18, 2016

Abstract

The influences and mechanisms of the physiology, rupture and reconstruction of the anterior cruciate

ligament (ACL) on kinematics and clinical outcomes have been investigated in many biomechanical and clinical studies over the last several decades. The knee is a complex joint with shifting contact points, pressures and axes that are affected when a ligament is injured. The ACL, as one of the intra-articular ligaments, has a strong influence on the resulting kinematics. Often, other meniscal or ligamentous injuries accompany ACL ruptures and further deteriorate the resulting kinematics and clinical outcomes. Knowing the surgical options, anatomic relations and current evidence to restore ACL function and considering the influence of concomitant injuries on resulting kinematics to restore full function can together help to achieve an optimal outcome.

Key words: Biomechanics; Anterior cruciate ligament; Joint pressure; Anterior cruciate ligament rupture; Graft fixation; Anterior cruciate ligament reconstruction

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This review of literature summarizes the influences and mechanisms of the physiology, rupture and reconstruction of the anterior cruciate ligament on kinematics and clinical outcomes. The major focuses are on the resulting joint kinematics after rupture and reconstruction and on biomechanics of graft fixation.

Domnick C, Raschke MJ, Herbert M. Biomechanics of the anterior cruciate ligament: Physiology, rupture and reconstruction techniques. *World J Orthop* 2016; 7(2): 82-93 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/82.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.82>

INTRODUCTION

Biomechanics is one major key to the function, stability and aging process of joints. The knee is a major and

complex joint. Its stability and motion are basically controlled by ligaments such as the anterior cruciate ligament (ACL)^[1].

The ACL is a central ligament of the knee. The main functional role of the ACL is to provide stability against anterior tibial translation (ATT) and internal rotation. An acute ACL rupture is a common orthopedic trauma, with an estimated incidence of 78 per 100000 persons and a mean age of 32 years in Sweden and an estimated incidence of up to 84 per 100000 persons in the United States^[2,3].

A common and frequent injury mechanism is non-contact combined valgus- and internal-rotation trauma^[2,4]. Therefore, ACL injuries are often associated with other ligamentous injuries, such as a (partial) rupture of the medial collateral ligament (MCL) or the menisci. In addition, compression of the lateral condyle with a bone bruise or chondral lesion is often associated with the injury due to the valgus trauma. Persistent instability of the knee may be associated with long-term degenerative lesions. Surgical treatment of the ACL in the context of other injured structures and reconstruction of the intact joint kinematics are suggested to be the keys to a good clinical outcome^[5,6].

ANATOMY

The ACL has its origin at the medial area of the lateral femoral condyle and inserts into the center of the eminentia of the tibia plateau next to the anterior horn of the lateral meniscus. The structure of the ACL has been described as two functional bundles: The anteromedial (AM) and the posterolateral (PL) bundle^[7]. These two bundles have been associated with different roles in anteroposterior and complex-rotational stabilization of the joint^[8-10]. The femoral origin was described as oval shaped with a longitudinal diameter of 18 mm and a width of approximately 11 mm^[11,12]. The AM bundle is inserted deep in the intercondylar notch directly in front of the intercondylar line and the edge of the chondral bone. The femoral insertion of the PL bundle is located at anterior of the AM bundle, also bordering the edge of the chondral bone. The tibial insertion of the AM bundle is located close to the anterior horn of the lateral meniscus at approximately the first 30% mark of a virtual sagittal line crossing the tibial plateau, while the PL bundle inserts slightly posterolateral to the AM bundle at approximately 44% of the virtual sagittal line^[9,13]. The anatomy of the ACL and functional bundles has been biomechanically evaluated in many studies^[8-10,14], and surgical techniques have evolved as a result. Due to the oval shape of the femoral condyles, the position of the joint axis varies during flexion in the sagittal plane^[15]. The oval/flat structure of the ACL plays an important role in stabilizing the knee joint under different flexion angles and, therefore, compensating for shifting knee flexion axes^[10,14,16]. The PL bundle has been shown to have particular stabilizing effects on the anteroposterior and rotational forces in near-to-extension positions

of less than 30°, whereas the AM bundle becomes tensioned and functional at higher flexion angles^[8,10,16]. Nevertheless, in a recent study, Kondo *et al.*^[14] found that the influence and reciprocal relationship of an insulated AM or PL bundle tear might have been overestimated. Recently, the existing knowledge of ACL anatomy was enhanced by a landmark anatomical study. Śmigielski *et al.*^[17] analyzed the detailed anatomical ACL structure of 111 human cadaveric knees. They found that femoral insertion and midsubstance of the ACL were thinner than previously assumed, and they determined a width of 11-17 mm and a thickness of only approximately 3 mm (Figure 1). Additionally, the tibial insertion site was recently anatomically analyzed by Siebold *et al.*^[18] and described as a "C"-shaped structure.

In addition to collagen fibers, nerves and mechanoreceptors are integrated within the ACL and play an important role in the proprioception of the joint^[19,20]. Nevertheless, there are more proprioceptive elements involved around the knee, such as other ligaments, muscles and the capsule.

KINEMATICS

Anterior tibial translation

In the intact knee, the ACL provides essential support for ATT and internal rotation. This functional role must be achieved at the base of the described anatomic insertion sites of the ACL, the complex oval-like shape of the condyles, and the tensile characteristics of the ligament^[15]. In extension, the ATT is low, with a maximum 2 mm scope, and provides support while standing. In flexion angles and when applying an external anteroposterior load, the ATT may increase up to 3 mm when walking and up to 5.5 mm under the anterior tibial load^[1].

When the ACL is ruptured or dissected, the ATT increases by up to 10 to 15 mm at 30° of knee flexion under 134 N of anterior load^[10,14,21]. Robotic/universal force-moment sensor (UFS) testing systems have been able to quantify passive ATT under the anterior tibial load in cadaveric knees at different flexion angles without being influenced by active muscle forces. Without these muscle forces, the highest increase in ATT was found between 15° and 40° of flexion. Clinically, ATT is often tested at different flexion angles. Stress radiographs, KT-1000 or rolimeters can help quantify the clinically observed ATT. The ischiocrural muscle group induces flexion by connecting the tuber ischiadicum with the proximal crus (pes anserinus tibia and fibular head). These muscle groups show a greater than 70° posterior force vector at 90° of knee flexion, which actively stabilizes against ATT (Figure 2). Considering these ligamentous and muscular kinematics, the ATT may therefore be clinically evaluated most accurately at near to extension angles (15° to 30°).

Cutting-edge studies have demonstrated an important role of the two functional ACL bundles for ATT and pivot shift at different flexion angles. In cadaveric studies, a

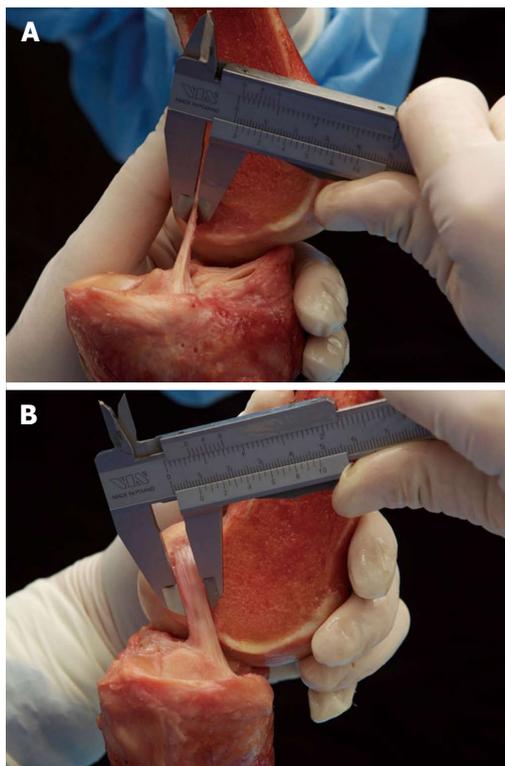


Figure 1 Śmigielski *et al*^[17] measuring the thickness (A) and width (B) of the “ribbon-like” midsubstance of the anterior cruciate ligament.

stabilizing role for the PL bundle in controlling the ATT at near-to-extension angles was found^[8,10,16]. The AM bundle seemed to have more influence in controlling higher flexion angles. Nevertheless, the suggested reciprocal relation of the two bundles is controversial and is still being discussed. A recent human cadaveric study by Kondo *et al*^[14] showed different results than prior studies: They reported that partial tears of the AM or the PL bundle showed a nonsignificant and less-than-expected increase of ATT. According to previous studies^[8,10,16], the tension of the PL bundle, as indicated by the distances of the bundle’s insertion sites, was increased at near-to-extension angles. Nevertheless, unlike others, Kondo *et al*^[14] found that AM bundle tensioning did not increase with growing flexion angles but stayed rather constant between 0° and 120° of flexion (Figure 3). Therefore, they concluded that when detecting a clinically unstable ATT in an examination of the knee, more than a partial (one-bundle) rupture of the ACL has to be assumed.

Rotational instability and pivot shift testing

Considering the anatomy of the ACL, its main structure has a complex diagonal route through the knee (anteroposterior and horizontal mediolateral fibers), which is almost reciprocal to the posterior cruciate ligament fibers^[22]. The role of the mediolateral ACL fibers might be versatile. In the intact knee, these fibers resist a complex internal tibial rotational force. Although a correlation between increased internal tibial rotation and deficient ACL seems obvious, the internal tibial rotation increases by less than 4°, from up to 30° of

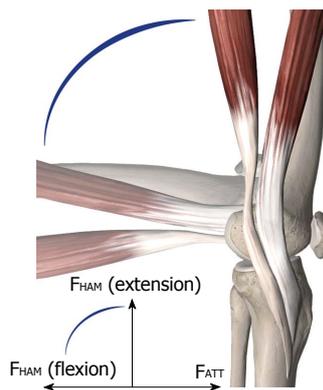


Figure 2 Semitendinosus and gracilis muscles with their insertions. At 90° of flexion, the forces of the hamstrings (F_{HAM}) are opposed to the anterior tibial translation (ATT) forces (F_{ATT}).

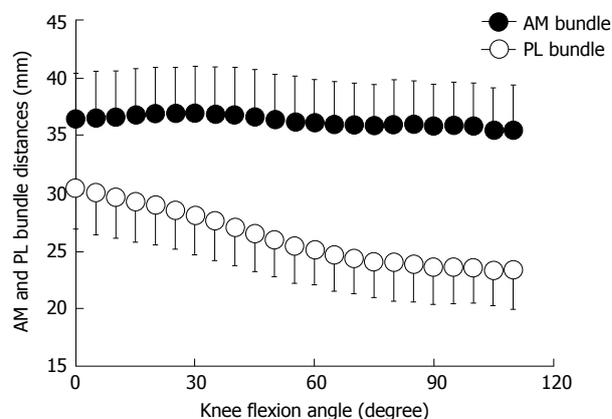


Figure 3 Distance between the femoral and tibial attachments of the anteromedial and posterolateral bundles of the anterior cruciate ligament during knee flexion (mean/SD) from Kondo *et al*^[14]. AM: Anteromedial; PL: Posterolateral.

internal rotation in the intact knee^[15], when the ACL is completely ruptured^[14,22], as other collateral ligaments are also important stabilizers against internal rotation^[23].

Although the resulting effect on isolated internal rotation stability seems small, the rotational axis of the knee alters from the center to a medial position near the pars intermedia of the internal meniscus when the ACL is ruptured^[24]. As a consequence, the movement in the lateral compartment increases (Figure 4).

Kanamori *et al*^[25] determined that both medial and lateral collateral ligaments compensate for *in situ* forces against internal rotation when the ACL is ruptured. Based on the effects of the medialized center of rotation with a subsequent increase of motion radius of the lateral compartment after an ACL rupture, the *in situ* forces of the posterolateral ligamentous structures increase by up to 413% at 15° of knee flexion^[25]. The influence of an ACL rupture on near-to-extension pivoting kinematics can be clinically assessed by the pivot shift test.

The pivot shift test is an established and valid clinical test for examining the ACL’s influence on complex rotational instability when ACL is ruptured^[26]. It not only is a dynamic knee instability test with a high specificity for ACL ruptures but also is influenced by active

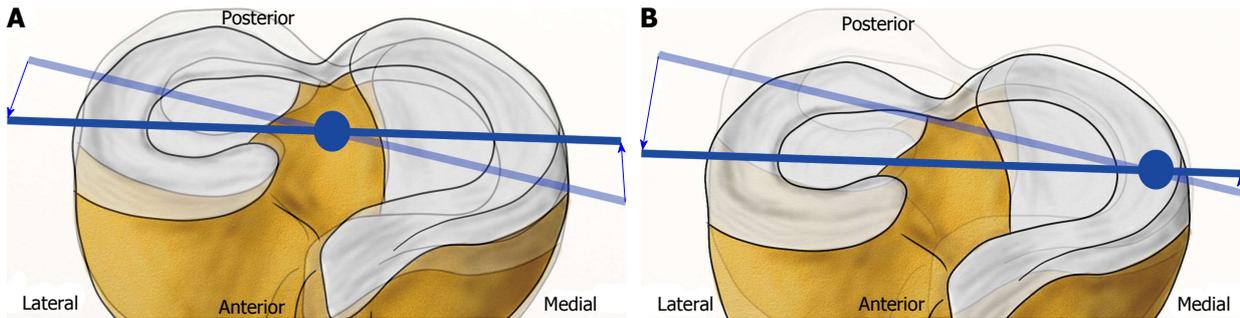


Figure 4 Shift of the center of the rotatory axis from the center/eminencia in an anterior cruciate ligament-intact knee (A) to a medial position (B). Modified from Amis *et al.*^[24].

muscle forces and by an inter-observer bias^[27]. Near extension the combined internal rotatory and valgus loads induces an anterolateral tibial subluxation in the ACL-deficient knee. With ongoing flexion, the collateral ligament apparatus and the iliotibial tractus reach tension at approximately 30° and retract the subluxated tibia^[26]. Biomechanically, the pivot shift examination can be simulated *in vitro* with a robotic/UFS system by applying combined internal rotatory (4-5 Nm) and valgus (10 Nm) loads while measuring the resulting anterolateral tibial translation^[8,21,22,28,29]. Several *in vitro* studies have demonstrated a correlation between a positive pivot shift phenomenon and a deficiency of horizontal (*e.g.*, PL bundle) fibers, as in the case of a steep PL-to-High-AM reconstruction^[8,10,16]. Clinically, the pivot shift phenomenon may be difficult to detect, especially in a situation of pain from an acute ACL tear and subsequent contraction of muscles, which can inhibit the subluxation phenomenon. Additionally, due to improving technologies, such as navigation and sensors, new techniques and tools have been developed to quantify clinical pivot shift kinematics^[30-32]. Although the pivot shift seems more complicated to evaluate compared to the ATT, studies report its strong correlation to clinical outcomes^[33]. In a clinical study of 63 patients with a follow-up at 5 to 9 years after ACL reconstruction surgery, Jonsson *et al.*^[34] found a positive correlation of the pivot shift phenomenon and osteoarthritic changes. Kocher *et al.*^[35] investigated the relationship between clinical assessment and different outcome parameter scores after ACL reconstruction surgery. While there was no correlation with investigated parameters regarding a positive ATT, a positive pivot shift was detected to be a significant predictor of satisfaction, giving way, difficulty in different types of activity, overall knee function, sports participation, and inferior Lysholm score.

Joint pressure

After an ACL rupture with a subsequent shift of the rotatory axis and increased instability, an altered intra-articular cartilage pressure seems obvious^[24]. Several biomechanical *in vivo* and *in vitro* studies have found decreased total joint pressure after an ACL rupture by pressure-sensitive sensors or electromyography driven model^[36-38]. As a possible consequence of decreased

joint pressure, the knee's flexion movement after an ACL rupture is also reduced^[37,39]. The complex kinematics of the knee joint and the altered strain of other ligamentous or cartilage structures suggest the importance of distinguishing the joint pressure in terms of its intra-articular sector, loading or passive condition and respective flexion angle^[15]. In the ACL-deficient knee, there is a shift of the rotatory axis to the medial compartment with slightly increased freedom of motion^[22,24]. Li *et al.*^[40] determined the tibiofemoral contact points during a one-legged lunge at different flexion angles in an *in vivo* study (Figure 5). They found out that there was a significant shift of the contact points on the tibial surface after an ACL rupture, most of them at flexion angles close to 15°. In the medial compartment, the contact points altered to a more posterior and more lateral position toward the intercondylar eminencia. In the lateral compartment, a lateralization of contact points was also observed but without alteration in the anteroposterior axis. While total patellofemoral joint pressure and the pressure of the medial patellofemoral compartment decrease after an ACL rupture, the lateral patellofemoral joint pressure increases at higher flexion angles above 60°^[36]. In a human cadaveric study, Imhauser *et al.*^[41] measured increased tibiofemoral contact forces in the posterior medial and lateral compartments under axial load and simulated Lachman and pivot shift tests after an ACL rupture (Figure 5).

In situ forces and tensile characteristics

In situ forces of the ACL have been calculated by Morrison^[42-44]. For normal walking, *in situ* forces of 169 N were observed. When descending stairs, increased *in situ* forces of 445 N were determined, which Morrison explained by the complementary effects of knee extensor muscles. Woo *et al.*^[45] performed tensile testing of young human cadaveric femur-ACL-tibia complexes and determined an ultimate load to failure of 2160 (\pm 157) N with a linear stiffness of 242 (\pm 28) N/mm.

INFLUENCE OF ACL RUPTURE ON OTHER STRUCTURES OF THE KNEE

A non-contact combined valgus- and internal-rotation trauma of the knee is described as one of the most

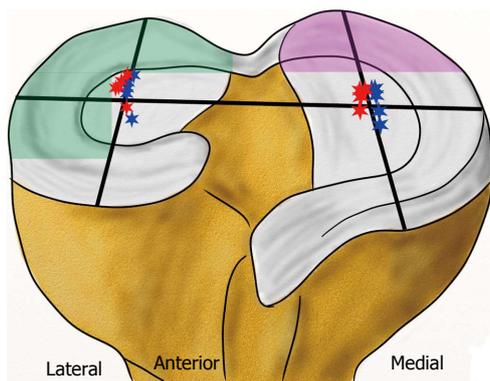


Figure 5 Lateral shift of femorotibial contact points at various flexion angles with intact anterior cruciate ligament (blue stars) and deficient anterior cruciate ligament (red stars) - modified from Li *et al*^[40]. Increased contact stress after an anterior cruciate ligament rupture in the posterior lateral compartment during pivot shifting (green area) and in the posterior medial compartment during Lachman testing (violet area) - modified from Imhauser *et al*^[41].

frequent mechanisms for an ACL rupture, as it may occur in pivoting sports such as in soccer or handball^[2,41]. This complex rotational trauma mechanism indicates that other structures should be examined to determine whether they were injured when an ACL rupture is suspected. The incidences of other accompanying injuries with the trauma mechanism and with altered kinematics of ACL rupture are detailed below.

MCL

MCL rupture is a frequent possible result of the valgus-stress component of a typical ACL trauma. The co-occurrence of MCL rupture was reported in every fifth case when the ACL was ruptured^[4,46]. An overseen and maintained medial instability after ACL reconstruction may result in inferior kinematics and persistent giving way, despite sufficient anteroposterior and pivot-rotational stability. In a clinical study, Zaffagnini *et al*^[47] found a persistent valgus instability after three years post ACL surgery and conservative treatment of a chronic MCL grade II rupture, but there was no difference in anteroposterior stability and in clinical outcome scores after three years compared to a surgically treated MCL. In another prospective randomized clinical study, Halinen *et al*^[48] also found equal stability and clinical outcome scores after operative or nonoperative treatment of concomitant MCL grade III lesions and combined ACL reconstruction in acute cases. Nevertheless, due to persistent instability, a higher risk for secondary graft failure after ACL reconstruction and for osteoarthritis is still discussed. Medial muscles, especially vastus medialis muscle, are considered to provide active stabilizing effects on medial instability. Therefore, alternative tendon grafts, other than the medial-inserting m. semitendinosus tendon, can be considered for ACL reconstruction, but the exact influence of the hamstring muscles has not yet been investigated.

Medial meniscus

Medial meniscus concomitant injuries are reported in

18%-54% of cases^[4,46,49,50] and have a comorbidity to acute and chronic ACL tears of up to 90%^[51]. A possible cause for this correlation in acute valgus- and internal-rotational trauma could be the mechanism of sudden medial instability with subsequent anteroposterior and rotational shear forces when the ACL ruptures. This shear trauma might even be enhanced by an accompanying MCL rupture^[4]. With persistent ACL instability, a shifted rotatory axis^[24] and contact points^[40] result in an altered flexion path of the medial femoral condyle and increase the risk for secondary injuries of the medial meniscus^[51,52]. Shear forces deriving from anteroposterior instability of the tibia will either extend the anterior displacement of the medial meniscus by up to 15 mm or result in compression forces on the meniscus^[10,14,21,24]. Decreased passive joint pressure within the medial compartment^[37,38] and combined instability seem to result in increased impact forces^[41] under stress, e.g., walking. Allen *et al*^[53] determined an increased peak yield of 50 N at 60° of flexion. The correlation of biomechanical influences between the ACL and the medial meniscus has been investigated in biomechanical human cadaveric studies. After dissection of the ACL and the medial meniscus, an increased ATT in contrast to a dissected ACL with an intact medial meniscus was found^[29,54].

Lateral meniscus

Lateral meniscus injuries are reported with concomitant rates of 17%-51%^[4,46,49,50], which is slightly less frequent than medial meniscus tears in cases of acute ACL rupture but also often caused by the typical valgus-internal-rotation trauma mechanism. The risk for a lateral meniscus injury seems to correlate with a coexisting lateral bone bruise, which is indicated on an MRI^[46]. Additionally, like the medial meniscus, the lateral meniscus provides significant stability. A deficient lateral meniscal root evokes pivot-rotational instability of the knee in cadaveric studies^[54,55].

Lateral collateral ligament

Lateral collateral ligament (LCL) concomitant injuries are rare and may be caused by anterolateral knee luxation injuries^[46]. Nevertheless, the LCL is an important stabilizer for the joint. Zantop *et al*^[56] have shown in a biomechanical study that a standalone ACL reconstruction cannot restore intact knee kinematics if the LCL is also deficient. Increased pivot-rotational anterolateral instability after an ACL rupture has promoted anatomical investigations of the anterolateral corner^[57]. Parsons *et al*^[58] found that the anterolateral ligament (ALL) provides stability against internal rotation at flexion angles greater than 35°. It has been proposed that a deficient ALL may correlate with a positive pivot shift sign. In addition, other structures of the anterolateral corner, such as the iliotibial tractus with its connecting Kaplan fibers, the lateral retinaculum and the lateral capsule, are suggested to influence pivot-rotational stability^[57]. Additionally, it is currently being discussed whether the ALL becomes insufficient over time in cases of chronic

Table 1 Biomechanical properties of tendons, grafts and fixation techniques

Subject	Maximum load to failure (N)	Stiffness (N/mm)	Ref.
Intact ACL (with femur and tibia)	2160 (\pm 157)	242 (\pm 28)	[45]
Two gracilis strands	1550 (\pm 369)	370 (\pm 108)	[69]
Two semitendinosus strands	2640 (\pm 320)	534 (\pm 76)	[69]
Four combined hamstring strands	4090 (\pm 295)	276 (\pm 204)	[69]
7 mm BPTB	2238 (\pm 316)	327 (\pm 58)	[67]
10 mm BPTB	2977 (\pm 516)	424/455 (\pm 57/67)	[67]
15 mm BPTB	4389 (\pm 708)	556 (\pm 67)	[67]
10 mm QTB	2353 (\pm 495)	621 (\pm 122)	[70]
Interference screw (BPTB)	683-863	76-80	[71]
Interference screw (hamstrings)	534-925	189-315	[68,72]
Endobutton (hamstrings)	520-1364	35-195	[68,73]
Interference screw and endobutton (hamstrings)	1290-1449	307-341	[68]

ACL: Anterior cruciate ligament; QTB: Quadriceps-tendon-bone; BPTB: Bone-patellar-tendon-bone.

ACL insufficiency^[59].

Secondary osteoarthritis

Secondary osteoarthritis is often observed after an ACL rupture: A meta-analysis by Ajuied *et al.*^[60] calculated a relative risk of 389 for radiographic osteoarthritic progression after an ACL rupture. There is good evidence for long-term degenerative progression and inferior clinical outcomes after concomitant meniscal and chondral injuries^[60,61]. Additionally, persistent pivot-rotational instability after an ACL rupture was found to be a predictor for osteoarthritis and subjective satisfaction^[33-35]. Nevertheless, although a positive effect of ACL reconstruction on osteoarthritic progression is proposed, to date there is no evidence for a preventive effect^[60,61].

ACL RECONSTRUCTION

ACL reconstruction is currently a topic of intense research, with more than 1940 hits in the Medline database for the term "ACL reconstruction" published within the past 5 years. Nevertheless, the history of ACL reconstruction goes back to the end of the 19th century. In 1895, Robson^[62] directly sewed the ACL in place *via* open medial arthrotomy. In 1903, Lange proposed an alloplastic ACL reconstruction with a silk graft^[5]. Grekow described in 1914 the first autologous transplant with a free iliotibial tractus stripe^[5]. From that moment, different autologous grafts have been used for transplantation. Brückner used a free patellar tendon graft for an arthroscopically assisted transplantation in 1966^[63]. Because of the high harvesting morbidity of the graft, the primary suture regained favor in the 1970s^[64,65]. Additionally, new synthetic materials (*e.g.*, Goretex, Carbonates) were used, but, due to complications, these alloplastic grafts, as well as the primary suture, were considered obsolete in the 1990s^[66]. Since then, arthroscopically assisted ACL

reconstruction with autologous or allogeneic tendon graft has evolved to worldwide acceptance.

Graft choice and graft fixation

Currently, hamstring-tendons (semitendinosus and gracilis), bone-patellar-tendon-bone (BPTB) complexes and quadriceps tendon-bone complexes are frequently used grafts. Tensile characteristics of these grafts are shown to be superior (maximum loads 2977 N^[67], 4140 N and 2353 N) to the native femur-ACL-tibia complex (2160 N)^[45] with similar stiffness (Table 1)^[45,67-73]. Nevertheless, the weakest point of primary graft failure has turned out to be the graft fixation (Table 1). There are many biomechanical studies that evaluate the biomechanical properties of graft fixation. Due to the scarcity of young human donors, animal or old human specimens have often been used, leading to results that may vary from those of typical young ACL reconstruction patients. Still, the dimensions of biomechanical properties range between the calculated *in situ* forces of the ACL^[42-44] and its ultimate failure load^[45]. In addition to sufficient failure loads of fixation techniques, fixation of the graft close to the insertion site is suggested to decrease longitudinal ("bungee") and sagittal ("windshield wiper") graft movements^[66,68]. Furthermore, Oh *et al.*^[68] have found significantly increased stiffness when an interference screw was added to an extracortical endobutton fixation (307 N/mm vs 195 N/mm).

Beyond biomechanics, clinical studies have shown good and comparable results with semitendinosus, quadriceps and bone-patellar-tendon-bone grafts for ACL reconstructions^[74-76]. Thus, it is feasible to make an individual graft choice - for instance, to avoid BPTB grafts when anterior knee pain is at risk (floor tiler) or to avoid semitendinosus grafts when concomitant medial collateral ligament injury exists. Novel minimally invasive surgical harvesting techniques for quadriceps tendons promise less cosmetic burden and more clinical acceptance^[77]. In a systematic review of overlapping meta-analyses, Mascarenhas *et al.*^[78] concluded that allografts were equal to autografts in terms of rerupture rates and clinical outcomes.

Tunnel positioning and effects on biomechanics

Until the beginning of the 21st century, ACL reconstruction with transtibial drilling of the femoral tunnel was the common surgical technique^[66]. As femoral tunnel placement depended on the tibial tunnel placement, it was difficult to aim for the anatomic ACL footprint of the lateral femur condyles through a tibial tunnel. The over-the-top position, with tunnel placement near the deep cartilage margin and the intercondylar roof, was preferred to achieve a good near-to-anatomic reconstruction^[66]. From an anatomical point of view, this position corresponds best to a near AM-bundle position. In 2002, Loh *et al.*^[79] were possibly the first to transform the known reciprocal relation of ACL bundles *in situ* forces into a cadaveric ACL reconstruction study. By drilling the femur in the 10 o'clock position, Loh intended

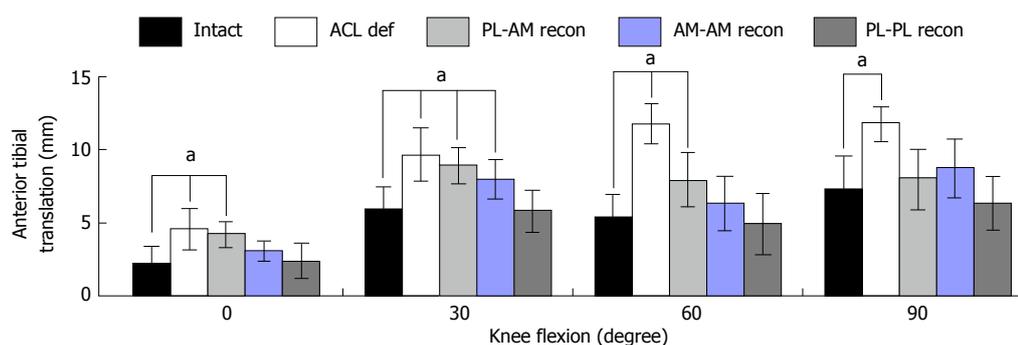


Figure 6 Anterior tibial translation under a simulated pivot shift test (combined 10 Nm valgus and 4 Nm internal rotational load, mean/SD, $^*P < 0.05$) as influenced by anterior cruciate ligament mismatch reconstruction of posterolateral and anteromedial bundles in a human cadaveric study by Herbolt *et al*^[8]. AM: Anteromedial; PL: Posterolateral; ACL: Anterior cruciate ligament.

to address PL-bundle fibers and evaluated the results against the conventional 11 o'clock over-the-top position. After evaluating resulting kinematics with a UFS/robotic testing system, the 10 o'clock reconstruction resulted in superior stability under combined rotatory loads. Consideration of anatomical ACL insertion sites continues to be a focus of biomechanical investigations. Mismatch reconstruction studies using robotic/UFS testing systems have demonstrated superior kinematics for combined rotatory loads and near-to-extension ATT when fibers of both the PL and AM bundles are reconstructed (Figure 6)^[8,16,21,80].

Most authors have concluded that the more horizontal fibers of the reconstructed PL bundle in particular were responsible for stabilizing the joint at near-to-extension angles.

With the "dependent" transtibial drilling technique, accurately and reliably addressing the femoral ACL footprint was very difficult^[81,82], although recently a novel modified transtibial technique was introduced that promises better aiming for the native footprint^[83]. Nevertheless, the introduction of the anteromedial portal technique allowed "independent" drilling of femoral ACL tunnels and, thus, a method to reliably and visually address the native tibial and femoral ACL footprints^[84,85]. Hence, novel anteromedial portal "anatomical" single- and double-bundle ACL reconstruction techniques have been clinically introduced and biomechanically evaluated^[21,86-89].

Correlating to the results of the biomechanical mismatch studies^[8,16], both anatomic double-bundle and anatomic single-bundle ACL reconstruction techniques resulted in superior kinematics compared to transtibial ("high-AM") femoral tunnel drilling for ACL reconstruction^[21,89,90]. In a human cadaveric study, Bedi *et al*^[91] determined that even an increased graft sized of a "high-AM" misplaced femoral ACL single bundle could not compensate for prime stability in contrast to a centrally placed smaller single bundle. However, in biomechanical studies, no superior kinematics could be found between anatomic double-bundle ACL reconstruction with drilling of an AM and a PL bundle tunnel in contrast to one centrally placed "anatomic" single-bundle

ACL reconstruction^[21,28,90]. Regardless, biomechanical advantages of "anatomic" double-bundle reconstruction may exist in larger knees: Siebold^[92] calculated better coverage of femoral ACL insertion sites larger than 16 mm with the double-bundle technique and good coverage of the femoral ACL footprint for sites smaller than 13 mm with the single-bundle technique.

From a clinical perspective, Chhabra *et al*^[93] and Griffith *et al*^[94] reported less tunnel expansion, decreased instability and fewer incidences of revision surgery after ACL reconstruction using the anteromedial portal technique compared to the transtibial technique. There have been many prospective randomized clinical studies comparing anatomic single- and double-bundle ACL reconstruction^[95,96]. Several of the clinical studies have shown minor but significant advantages for the anatomic double-bundle technique. In their meta-analysis, Desai *et al*^[96] included 15 prospective clinical trials and found that 3 of those indicated significant superior anteroposterior stability of the anatomic double-bundle group in contrast to the anatomic single-bundle group. Furthermore, 2 of the included clinical studies resulted in superior pivot-rotational stability^[96]. Regarding clinical outcome scores, van Eck *et al*^[95] reported in their meta-analysis of 12 prospective clinical studies that no significantly different parameters of IKDC score, Lysholm score, range of motion and complication rate between anatomic double-bundle and anatomic single-bundle were detected. Despite these good biomechanical and clinical results, the anatomic double-bundle ACL reconstruction is controversial. In contrast to anatomic single-bundle reconstruction, its upfront costs are more expensive^[97], and the surgical technique and tunnel revision surgery are considered to be more sophisticated^[98].

New trends and concepts in ACL reconstruction surgery

Trying to simulate anatomic ACL insertion sites has resulted in good biomechanical and clinical parameters over the last decade. To mimic the effect of the anatomic double-bundle technique to effectively address both the PL and the AM bundle for femoral tunnel drilling, Herbolt *et al*^[99] introduced a rectangular tunnel technique, which is supposed to show better coverage of both bundle

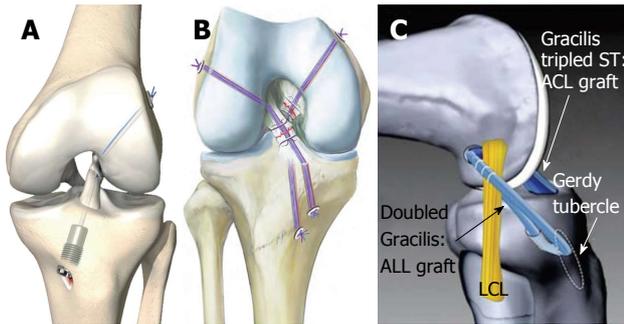


Figure 7 Novel anterior cruciate ligament repair techniques. A: Anterior cruciate ligament (ACL) suture and dynamic augmentation (Ligamys™, copyright Mathys Ltd., Bettlach, Switzerland); B: Ligament bracing (from Heitmann *et al.*^[104]); C: ACL reconstruction with anterolateral ligament (ALL) augmentation (from Sonnery-Cottet *et al.*^[59]). ST: Semitendinosus, LCL: Lateral collateral ligament.

insertions with one single, regular-sized transplant. Their biomechanical human cadaveric study resulted in superior ATT stability in contrast to a conventional round-tunnel, single-bundle reconstruction at 0° and 15° of flexion^[99]. Sonnery-Cottet *et al.*^[59] and Kittl *et al.*^[57] reported a combined ACL and ALL reconstruction technique (with tenodesis) to improve the stability of the anterolateral corner in cases of acute or chronic ACL rupture with increased anterolateral rotational instability (Figure 7C). An initial case study of 92 patients resulted in significantly improved pivot-rotational stability after 2 years^[59]. However, prospective randomized clinical studies to distinguish the pivot-rotational stabilizing effects between a conventional ACL reconstruction and a combined ACL/ALL reconstruction are still lacking. Primary suture with or without alloplastic augmentation of the ruptured ACL has resulted in inferior clinical outcomes in prospective and retrospective studies^[66,100]. The majority of these alloplastic augmentations have been stiff constructs in a nonanatomical position (over-the-top position or extra-articular)^[66,100]. However, with the aim to restore proprioceptive properties of the ligament and to avoid the harvesting morbidity of tendon grafts, Egli *et al.*^[101], and Kohl *et al.*^[102] have introduced a new method of primary suturing of a traumatic ACL rupture with combined dynamic alloplastic intraligamentous stabilization (Figure 7A). To avoid mechanical fatigue of the augmentation and to adapt to the complex flexion axis of the knee^[15], the augmentation cord is placed near-anatomical within or slightly behind the ACL and dynamically suspended by an intraosseous spring mechanism. Initial small-sample clinical studies after suturing with dynamic alloplastic intraligamentous stabilization have shown promising results for primary ACL ruptures and for combined suturing and augmentation of other structures for complex knee dislocation injuries^[101,103].

Heitmann *et al.*^[104] described a similar technique with suturing and anatomically placed intraligamentous alloplastic augmentation of torn cruciate ligaments in cases of acute knee dislocation injury (Figure 7B). The authors exclusively recommend the technique for

acute knee dislocations injuries of Schenck III and IV types that do not involve a dynamic suspension of the augmentation. An initial clinical study of 20 patients showed satisfying results one year after surgery^[104].

The perspective of suturing for preserving autologous graft material and the native ACL has often been considered to reduce morbidity in the past, but the results were not promising^[66,100]. For complex ligamentous knee dislocation injuries, there seems to be a good potential for reduced harvesting morbidity and OR time. Additionally, it remains unclear whether a dynamic or a static augmentation suture in a combined cruciate ligament injury was best either for restoring stability or not inducing deficits of range-of-motion or misplacing the physiological axes of the knee. To date, there are no data from prospective randomized controlled studies.

CONCLUSION

The knee is a complex joint with shifting contact points, pressures and axes that are affected when a ligament is injured. The ACL, as one of the intra-articular ligaments, has a strong influence on the resulting kinematics. Often, other meniscal or ligamentous injuries accompany ACL rupture and further deteriorate resulting kinematics and clinical outcomes. Knowing the surgical options, anatomic relations and current evidence to restore ACL function and considering the influence of concomitant injuries on resulting kinematics to restore full function together can help to achieve an optimal outcome.

REFERENCES

- 1 **Markolf KL**, Mensch JS, Amstutz HC. Stiffness and laxity of the knee--the contributions of the supporting structures. A quantitative in vitro study. *J Bone Joint Surg Am* 1976; **58**: 583-594 [PMID: 946969]
- 2 **Nordenvall R**, Bahmanyar S, Adami J, Stenros C, Wredmark T, Felländer-Tsai L. A population-based nationwide study of cruciate ligament injury in Sweden, 2001-2009: incidence, treatment, and sex differences. *Am J Sports Med* 2012; **40**: 1808-1813 [PMID: 22684536 DOI: 10.1177/0363546512449306]
- 3 **Griffin LY**, Albohm MJ, Arendt EA, Bahr R, Beynon BD, Demajo M, Dick RW, Engebretsen L, Garrett WE, Hannafin JA, Hewett TE, Huston LJ, Ireland ML, Johnson RJ, Lephart S, Mandelbaum BR, Mann BJ, Marks PH, Marshall SW, Myklebust G, Noyes FR, Powers C, Shields C, Shultz SJ, Silvers H, Slauterbeck J, Taylor DC, Teitz CC, Wojtyk EM, Yu B. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II Meeting. 2005: 1512-1532
- 4 **Bates NA**, McPherson AL, Rao MB, Myer GD, Hewett TE. Characteristics of inpatient anterior cruciate ligament reconstructions and concomitant injuries. *Knee Surg Sports Traumatol Arthrosc* 2014; Epub ahead of print [PMID: 25510363 DOI: 10.1007/s00167-014-3478-3]
- 5 **Eberhardt C**, Jäger A, Schwetlick G, Rauschmann MA. [History of surgery of the anterior cruciate ligament]. *Orthopade* 2002; **31**: 702-709 [PMID: 12426748 DOI: 10.1007/s00132-002-0329-6]
- 6 **Zysk SP**, Refior HJ. Operative or conservative treatment of the acutely torn anterior cruciate ligament in middle-aged patients. A follow-up study of 133 patients between the ages of 40 and 59 years. *Arch Orthop Trauma Surg* 2000; **120**: 59-64 [PMID: 10653106]

- 7 **Weber W**, Weber E. Mechanics of the Human Walking Apparatus. Springer Verlag, 1992: 75-92
- 8 **Herbort M**, Lenschow S, Fu FH, Petersen W, Zantop T. ACL mismatch reconstructions: influence of different tunnel placement strategies in single-bundle ACL reconstructions on the knee kinematics. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1551-1558 [PMID: 20461359 DOI: 10.1007/s00167-010-1163-8]
- 9 **Petersen W**, Zantop T. Anatomy of the anterior cruciate ligament with regard to its two bundles. *Clin Orthop Relat Res* 2007; **454**: 35-47 [PMID: 17075382 DOI: 10.1097/BLO.0b013e31802b4a59]
- 10 **Zantop T**, Herbort M, Raschke MJ, Fu FH, Petersen W. The role of the anteromedial and posterolateral bundles of the anterior cruciate ligament in anterior tibial translation and internal rotation. *Am J Sports Med* 2007; **35**: 223-227 [PMID: 17158275 DOI: 10.1177/0363546506294571]
- 11 **Sasaki N**, Ishibashi Y, Tsuda E, Yamamoto Y, Maeda S, Mizukami H, Toh S, Yagihashi S, Tonosaki Y. The femoral insertion of the anterior cruciate ligament: discrepancy between macroscopic and histological observations. *Arthroscopy* 2012; **28**: 1135-1146 [PMID: 22440794 DOI: 10.1016/j.arthro.2011.12.021]
- 12 **Odensten M**, Gillquist J. Functional anatomy of the anterior cruciate ligament and a rationale for reconstruction. *J Bone Joint Surg Am* 1985; **67**: 257-262 [PMID: 3968118]
- 13 **Siebold R**, Ellert T, Metz S, Metz J. Tibial insertions of the anteromedial and posterolateral bundles of the anterior cruciate ligament: morphometry, arthroscopic landmarks, and orientation model for bone tunnel placement. *Arthroscopy* 2008; **24**: 154-161 [PMID: 18237698 DOI: 10.1016/j.arthro.2007.08.006]
- 14 **Kondo E**, Merican AM, Yasuda K, Amis AA. Biomechanical analysis of knee laxity with isolated anteromedial or posterolateral bundle-deficient anterior cruciate ligament. *Arthroscopy* 2014; **30**: 335-343 [PMID: 24581258 DOI: 10.1016/j.arthro.2013.12.003]
- 15 **Freeman MA**, Pinskerova V. The movement of the normal tibio-femoral joint. *J Biomech* 2005; **38**: 197-208 [PMID: 15598446 DOI: 10.1016/j.jbiomech.2004.02.006]
- 16 **Kato Y**, Maeyama A, Lertwanich P, Wang JH, Ingham SJ, Kramer S, Martins CQ, Smolinski P, Fu FH. Biomechanical comparison of different graft positions for single-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 816-823 [PMID: 22419266 DOI: 10.1007/s00167-012-1951-4]
- 17 **Śmigielski R**, Zdanowicz U, Drwięga M, Ciszek B, Ciszowska-Lysoń B, Siebold R. Ribbon like appearance of the midsubstance fibres of the anterior cruciate ligament close to its femoral insertion site: a cadaveric study including 111 knees. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3143-3150 [PMID: 24972997 DOI: 10.1007/s00167-014-3146-7]
- 18 **Siebold R**, Schuhmacher P, Fernandez F, Śmigielski R, Fink C, Brehmer A, Kirsch J. Flat midsubstance of the anterior cruciate ligament with tibial "C"-shaped insertion site. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3136-3142 [PMID: 24841941 DOI: 10.1007/s00167-014-3058-6]
- 19 **Bali K**, Dhillon MS, Vasistha RK, Kakkar N, Chana R, Prabhakar S. Efficacy of immunohistological methods in detecting functionally viable mechanoreceptors in the remnant stumps of injured anterior cruciate ligaments and its clinical importance. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 75-80 [PMID: 21541706 DOI: 10.1007/s00167-011-1526-9]
- 20 **Iwasa J**, Ochi M, Uchio Y, Adachi N, Kawasaki K. Decrease in anterior knee laxity by electrical stimulation of normal and reconstructed anterior cruciate ligaments. *J Bone Joint Surg Br* 2006; **88**: 477-483 [PMID: 16567782 DOI: 10.1302/0301-620X.88B4.17186]
- 21 **Kondo E**, Merican AM, Yasuda K, Amis AA. Biomechanical comparison of anatomic double-bundle, anatomic single-bundle, and nonanatomic single-bundle anterior cruciate ligament reconstructions. *Am J Sports Med* 2011; **39**: 279-288 [PMID: 21239692 DOI: 10.1177/0363546510392350]
- 22 **Diermann N**, Schumacher T, Schanz S, Raschke MJ, Petersen W, Zantop T. Rotational instability of the knee: internal tibial rotation under a simulated pivot shift test. *Arch Orthop Trauma Surg* 2009; **129**: 353-358 [PMID: 18594847 DOI: 10.1007/s00402-008-0681-z]
- 23 **Kim YH**, Purevsuren T, Kim K, Oh KJ. Contribution of posterolateral corner structures to knee joint translational and rotational stabilities: a computational study. *Proc Inst Mech Eng H* 2013; **227**: 968-975 [PMID: 23736993 DOI: 10.1177/0954411913490456]
- 24 **Amis AA**, Bull AMJ, Lie DTT. Biomechanics of rotational instability and anatomic anterior cruciate ligament reconstruction. *Oper Tech Orthop* 2005; **15**: 29-35 [DOI: 10.1053/j.oto.2004.10.009]
- 25 **Kanamori A**, Sakane M, Zeminski J, Rudy TW, Woo SL. In-situ force in the medial and lateral structures of intact and ACL-deficient knees. *J Orthop Sci* 2000; **5**: 567-571 [PMID: 11180920]
- 26 **Galway HR**, MacIntosh DL. The lateral pivot shift: a symptom and sign of anterior cruciate ligament insufficiency. *Clin Orthop Relat Res* 1980; **(147)**: 45-50 [PMID: 7371314]
- 27 **Bull A**, Amis AA. The pivot-shift phenomenon: a clinical and biomechanical perspective. *The Knee* 1998; **5**: 141-158 [DOI: 10.1016/s0968-0160(97)10027-8]
- 28 **Goldsmith MT**, Jansson KS, Smith SD, Engebretsen L, LaPrade RF, Wijdicks CA. Biomechanical comparison of anatomic single- and double-bundle anterior cruciate ligament reconstructions: an in vitro study. *Am J Sports Med* 2013; **41**: 1595-1604 [PMID: 23696212 DOI: 10.1177/0363546513487065]
- 29 **Lorbach O**, Kieb M, Domnick C, Herbort M, Weyers I, Raschke M, Engelhardt M. Biomechanical evaluation of knee kinematics after anatomic single- and anatomic double-bundle ACL reconstructions with medial meniscal repair. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2734-2741 [PMID: 24850240 DOI: 10.1007/s00167-014-3071-9]
- 30 **Araujo PH**, Ahlden M, Hoshino Y, Muller B, Moloney G, Fu FH, Musahl V. Comparison of three non-invasive quantitative measurement systems for the pivot shift test. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 692-697 [PMID: 22218829 DOI: 10.1007/s00167-011-1862-9]
- 31 **Pearle AD**, Kendoff D, Musahl V, Warren RF. The pivot-shift phenomenon during computer-assisted anterior cruciate ligament reconstruction. *J Bone Joint Surg Am* 2009; **91** Suppl 1: 115-118 [PMID: 19182036 DOI: 10.2106/JBJS.H.01553]
- 32 **Lorbach O**, Kieb M, Brogard P, Maas S, Pape D, Seil R. Static rotational and sagittal knee laxity measurements after reconstruction of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 844-850 [PMID: 21811853 DOI: 10.1007/s00167-011-1635-5]
- 33 **Ayeni OR**, Chahal M, Tran MN, Sprague S. Pivot shift as an outcome measure for ACL reconstruction: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 767-777 [PMID: 22218828 DOI: 10.1007/s00167-011-1860-y]
- 34 **Jonsson H**, Riklund-Ahlström K, Lind J. Positive pivot shift after ACL reconstruction predicts later osteoarthritis: 63 patients followed 5-9 years after surgery. *Acta Orthop Scand* 2004; **75**: 594-599 [PMID: 15513493 DOI: 10.1080/00016470410001484]
- 35 **Kocher MS**. Relationships Between Objective Assessment of Ligament Stability and Subjective Assessment of Symptoms and Function After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2004; **32**: 629-634 [DOI: 10.1177/0363546503261722]
- 36 **Tajima G**, Iriuchishima T, Ingham SJ, Shen W, van Houten AH, Aerts MM, Shimamura T, Smolinski P, Fu FH. Anatomic double-bundle anterior cruciate ligament reconstruction restores patellofemoral contact areas and pressures more closely than nonanatomic single-bundle reconstruction. *Arthroscopy* 2010; **26**: 1302-1310 [PMID: 20887929 DOI: 10.1016/j.arthro.2010.01.034]
- 37 **Gardinier ES**, Manal K, Buchanan TS, Snyder-Mackler L. Altered loading in the injured knee after ACL rupture. *J Orthop Res* 2012; **31**: 458-464 [DOI: 10.1002/jor.22249]
- 38 **Khandha A**, Gardinier E, Capin J, Manal K, Snyder-Mackler L, Buchanan T. Do decreased medial compartment contact forces and loading asymmetries exist after anterior cruciate ligament reconstruction and rehabilitation? - a 5 year follow-up study. *Osteoarthritis Cartilage* 2014; **22**: S103 [DOI: 10.1016/j.joca.2014.02.194]

- 39 **Hart JM**, Ko JW, Konold T, Pietrosimone B. Sagittal plane knee joint moments following anterior cruciate ligament injury and reconstruction: a systematic review. *Clin Biomech* (Bristol, Avon) 2010; **25**: 277-283 [PMID: 20097459 DOI: 10.1016/j.clinbiomech.2009.12.004]
- 40 **Li G**, Moses JM, Papannagari R, Pathare NP, DeFrate LE, Gill TJ. Anterior cruciate ligament deficiency alters the in vivo motion of the tibiofemoral cartilage contact points in both the anteroposterior and mediolateral directions. *J Bone Joint Surg Am* 2006; **88**: 1826-1834 [PMID: 16882908 DOI: 10.2106/JBJS.E.00539]
- 41 **Imhauser C**, Mauro C, Choi D, Rosenberg E, Mathew S, Nguyen J, Ma Y, Wickiewicz T. Abnormal tibiofemoral contact stress and its association with altered kinematics after center-center anterior cruciate ligament reconstruction: an in vitro study. *Am J Sports Med* 2013; **41**: 815-825 [PMID: 23470858 DOI: 10.1177/0363546512475205]
- 42 **Morrison JB**. The mechanics of the knee joint in relation to normal walking. *J Biomech* 1970; **3**: 51-61 [PMID: 5521530]
- 43 **Dargel J**, Gotter M, Mader K, Pennig D, Koebke J, Schmidt-Wiethoff R. Biomechanics of the anterior cruciate ligament and implications for surgical reconstruction. *Strategies Trauma Limb Reconstr* 2007; **2**: 1-12 [PMID: 18427909 DOI: 10.1007/s11751-007-0016-6]
- 44 **Morrison JB**. Function of the knee joint in various activities. *Biomed Eng* 1969; **4**: 573-580 [PMID: 5378020]
- 45 **Woo SL**, Hollis JM, Adams DJ, Lyon RM, Takai S. Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation. *Am J Sports Med* 1991; **19**: 217-225 [PMID: 1867330]
- 46 **Yoon KH**, Yoo JH, Kim KI. Bone contusion and associated meniscal and medial collateral ligament injury in patients with anterior cruciate ligament rupture. *J Bone Joint Surg Am* 2011; **93**: 1510-1518 [PMID: 22204006 DOI: 10.2106/JBJS.J.01320]
- 47 **Zaffagnini S**, Bonanzinga T, Marcheggiani Muccioli GM, Giordano G, Bruni D, Bignozzi S, Lopomo N, Marcacci M. Does chronic medial collateral ligament laxity influence the outcome of anterior cruciate ligament reconstruction?: a prospective evaluation with a minimum three-year follow-up. *J Bone Joint Surg Br* 2011; **93**: 1060-1064 [PMID: 21768629 DOI: 10.1302/0301-620X.93B8.26183]
- 48 **Halinen J**, Lindahl J, Hirvensalo E, Santavirta S. Operative and nonoperative treatments of medial collateral ligament rupture with early anterior cruciate ligament reconstruction: a prospective randomized study. *Am J Sports Med* 2006; **34**: 1134-1140 [PMID: 16452264 DOI: 10.1177/0363546505284889]
- 49 **Forkel P**, Reuter S, Sprenger F, Achtenich A, Herbst E, Imhoff A, Petersen W. Different patterns of lateral meniscus root tears in ACL injuries: application of a differentiated classification system. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 112-118 [PMID: 25502611 DOI: 10.1007/s00167-014-3467-6]
- 50 **Gadeyne S**, Besse JL, Galand-Desme S, Lerat JL, Moyen B. [Analysis of meniscal lesions accompanying anterior cruciate ligament tears: A retrospective analysis of 156 patients]. *Rev Chir Orthop Reparatrice Appar Mot* 2006; **92**: 448-454 [PMID: 17088738]
- 51 **Jiang W**, Gao SG, Li KH, Luo L, Li YS, Luo W, Lei GH. Impact of Partial and complete rupture of anterior cruciate ligament on medial meniscus: A cadaveric study. *Indian J Orthop* 2012; **46**: 514-519 [PMID: 23162142 DOI: 10.4103/0019-5413.101040]
- 52 **Krych AJ**, Pitts RT, Dajani KA, Stuart MJ, Levy BA, Dahm DL. Surgical repair of meniscal tears with concomitant anterior cruciate ligament reconstruction in patients 18 years and younger. *Am J Sports Med* 2010; **38**: 976-982 [PMID: 20299545 DOI: 10.1177/0363546509354055]
- 53 **Allen CR**, Wong EK, Livesay GA, Sakane M, Fu FH, Woo SL. Importance of the medial meniscus in the anterior cruciate ligament-deficient knee. *J Orthop Res* 2000; **18**: 109-115 [PMID: 10716286 DOI: 10.1002/jor.1100180116]
- 54 **Musahl V**, Citak M, O'Loughlin PF, Choi D, Bedi A, Pearle AD. The effect of medial versus lateral meniscectomy on the stability of the anterior cruciate ligament-deficient knee. *Am J Sports Med* 2010; **38**: 1591-1597 [PMID: 20530720 DOI: 10.1177/0363546510364402]
- 55 **Shybut TB**, Vega CE, Haddad J, Alexander JW, Gold JE, Noble PC, Lowe WR. Effect of lateral meniscal root tear on the stability of the anterior cruciate ligament-deficient knee. *Am J Sports Med* 2015; **43**: 905-911 [PMID: 25589386 DOI: 10.1177/0363546514563910]
- 56 **Zantop T**, Schumacher T, Schanz S, Raschke MJ, Petersen W. Double-bundle reconstruction cannot restore intact knee kinematics in the ACL/LCL-deficient knee. *Arch Orthop Trauma Surg* 2010; **130**: 1019-1026 [PMID: 20217104 DOI: 10.1007/s00402-010-1081-8]
- 57 **Kittl C**, Weiler A, Amis AA. Anterolateral rotatory instability. *Arthroscopie* 2014; **27**: 170-176 [DOI: 10.1007/s00142-014-0816-x]
- 58 **Parsons EM**, Gee AO, Spiekerman C, Cavanagh PR. The biomechanical function of the anterolateral ligament of the knee. *Am J Sports Med* 2015; **43**: 669-674 [PMID: 25556221 DOI: 10.1177/0363546514562751]
- 59 **Sonnery-Cottet B**, Thauinat M, Freychet B, Pupim BH, Murphy CG, Claes S. Outcome of a Combined Anterior Cruciate Ligament and Anterolateral Ligament Reconstruction Technique With a Minimum 2-Year Follow-up. *Am J Sports Med* 2015; **43**: 1598-1605 [PMID: 25740835 DOI: 10.1177/0363546515571571]
- 60 **Ajuied A**, Wong F, Smith C, Norris M, Earnshaw P, Back D, Davies A. Anterior cruciate ligament injury and radiologic progression of knee osteoarthritis: a systematic review and meta-analysis. *Am J Sports Med* 2014; **42**: 2242-2252 [PMID: 24214929 DOI: 10.1177/0363546513508376]
- 61 **Abermann E**, Hoser C, Benedetto KP, Hepperger C, Fink C. Development of osteoarthritis after anterior cruciate ligament rupture. *Arthroscopie* 2015; **28**: 26-30 [DOI: 10.1007/s00142-014-0835-7]
- 62 **Robson AW**. VI. Ruptured Crucial Ligaments and their Repair by Operation. *Ann Surg* 1903; **37**: 716-718 [PMID: 17861289]
- 63 **Wirth CJ**, Artmann M, J ger M, Refior HJ. Plastic reconstruction of old anterior cruciate ligament ruptures by the Brueckner procedure. *Arch orthop Unfall-Chir* 1974; **78**: 362-73 [DOI: 10.1007/BF00415817]
- 64 **Feagin JA**, Curl WW. Isolated tear of the anterior cruciate ligament: 5-year follow-up study. *Am J Sports Med* 1976; **4**: 95-100 [PMID: 984289]
- 65 **Odensten M**, Lysholm J, Gillquist J. Suture of fresh ruptures of the anterior cruciate ligament. A 5-year follow-up. *Acta Orthop Scand* 1984; **55**: 270-272 [PMID: 6377805]
- 66 **Fu FH**, Bennett CH, Ma CB, Menetrey J, Lattermann C. Current trends in anterior cruciate ligament reconstruction. Part II. Operative procedures and clinical correlations. *Am J Sports Med* 2000; **28**: 124-130 [PMID: 10653557]
- 67 **Cooper DE**, Deng XH, Burstein AL, Warren RF. The strength of the central third patellar tendon graft. A biomechanical study. *Am J Sports Med* 1993; **21**: 818-823; discussion 823-824 [PMID: 8291632]
- 68 **Oh YH**, Namkoong S, Strauss EJ, Ishak C, Hecker AT, Jazrawi LM, Rosen J. Hybrid femoral fixation of soft-tissue grafts in anterior cruciate ligament reconstruction using the EndoButton CL and bioabsorbable interference screws: a biomechanical study. *Arthroscopy* 2006; **22**: 1218-1224 [PMID: 17084300 DOI: 10.1016/j.arthro.2006.07.022]
- 69 **Hammer DL**, Brown CH, Steiner ME, Hecker AT, Hayes WC. Hamstring tendon grafts for reconstruction of the anterior cruciate ligament: biomechanical evaluation of the use of multiple strands and tensioning techniques. *J Bone Joint Surg Am* 1999; **81**: 549-557 [PMID: 10225801 DOI: 10.4103/2277-9175.98566]
- 70 **Stäubli HU**, Schatzmann L, Brunner P, Rincón L, Nolte LP. Quadriceps tendon and patellar ligament: cryosectional anatomy and structural properties in young adults. *Knee Surg Sports Traumatol Arthrosc* 1996; **4**: 100-110 [PMID: 8884731]
- 71 **Kousa P**, Järvinen TL, Kannus P, Järvinen M. Initial fixation

- strength of bioabsorbable and titanium interference screws in anterior cruciate ligament reconstruction. Biomechanical evaluation by single cycle and cyclic loading. *Am J Sports Med* 2001; **29**: 420-425 [PMID: 11476379]
- 72 **Kousa P**, Järvinen TL, Vihavainen M, Kannus P, Järvinen M. The fixation strength of six hamstring tendon graft fixation devices in anterior cruciate ligament reconstruction. Part I: femoral site. *Am J Sports Med* 2003; **31**: 174-181 [PMID: 12642249]
- 73 **Höher J**, Scheffler S, Weiler A. Graft choice and graft fixation in PCL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2003; **11**: 297-306 [PMID: 12942234 DOI: 10.1007/s00167-003-0408-1]
- 74 **Barenius B**, Ponzer S, Shalabi A, Bujak R, Norlén L, Eriksson K. Increased risk of osteoarthritis after anterior cruciate ligament reconstruction: a 14-year follow-up study of a randomized controlled trial. *Am J Sports Med* 2014; **42**: 1049-1057 [PMID: 24644301 DOI: 10.1177/0363546514526139]
- 75 **Slone HS**, Romine SE, Premkumar A, Xerogeanes JW. Quadriceps tendon autograft for anterior cruciate ligament reconstruction: a comprehensive review of current literature and systematic review of clinical results. *Arthroscopy* 2015; **31**: 541-554 [PMID: 25543249 DOI: 10.1016/j.arthro.2014.11.010]
- 76 **Sajovic M**, Strahovnik A, Dernovsek MZ, Skaza K. Quality of life and clinical outcome comparison of semitendinosus and gracilis tendon versus patellar tendon autografts for anterior cruciate ligament reconstruction: an 11-year follow-up of a randomized controlled trial. *Am J Sports Med* 2011; **39**: 2161-2169 [PMID: 21712483 DOI: 10.1177/0363546511411702]
- 77 **Fink C**, Herbort M, Abermann E, Hoser C. Minimally invasive harvest of a quadriceps tendon graft with or without a bone block. *Arthrosc Tech* 2014; **3**: e509-e513 [PMID: 25264512 DOI: 10.1016/j.eats.2014.06.003]
- 78 **Mascarenhas R**, Erickson BJ, Sayegh ET, Verma NN, Cole BJ, Bush-Joseph C, Bach BR. Is there a higher failure rate of allografts compared with autografts in anterior cruciate ligament reconstruction: a systematic review of overlapping meta-analyses. *Arthroscopy* 2015; **31**: 364-372 [PMID: 25220350 DOI: 10.1016/j.arthro.2014.07.011]
- 79 **Loh JC**, Fukuda Y, Tsuda E, Steadman RJ, Fu FH, Woo SL. Knee stability and graft function following anterior cruciate ligament reconstruction: Comparison between 11 o'clock and 10 o'clock femoral tunnel placement. 2002 Richard O'Connor Award paper. *Arthroscopy* 2003; **19**: 297-304 [PMID: 12627155 DOI: 10.1053/jars.2003.50084]
- 80 **Driscoll MD**, Isabell GP, Conditt MA, Ismaily SK, Jupiter DC, Noble PC, Lowe WR. Comparison of 2 femoral tunnel locations in anatomic single-bundle anterior cruciate ligament reconstruction: a biomechanical study. *Arthroscopy* 2012; **28**: 1481-1489 [PMID: 22796141 DOI: 10.1016/j.arthro.2012.03.019]
- 81 **Kopf S**, Forsythe B, Wong AK, Tashman S, Anderst W, Irrgang JJ, Fu FH. Nonanatomic tunnel position in traditional transtibial single-bundle anterior cruciate ligament reconstruction evaluated by three-dimensional computed tomography. *J Bone Joint Surg Am* 2010; **92**: 1427-1431 [PMID: 20516318 DOI: 10.2106/JBJS.1.00655]
- 82 **Piasecki DP**, Bach BR, Espinoza Orias AA, Verma NN. Anterior cruciate ligament reconstruction: can anatomic femoral placement be achieved with a transtibial technique? *Am J Sports Med* 2011; **39**: 1306-1315 [PMID: 21335345 DOI: 10.1177/0363546510397170]
- 83 **Youn YS**, Cho SD, Lee SH, Youn CH. Modified transtibial versus anteromedial portal technique in anatomic single-bundle anterior cruciate ligament reconstruction: comparison of femoral tunnel position and clinical results. *Am J Sports Med* 2014; **42**: 2941-2947 [PMID: 25269655 DOI: 10.1177/0363546514551922]
- 84 **Harner CD**, Honkamp NJ, Ranawat AS. Anteromedial portal technique for creating the anterior cruciate ligament femoral tunnel. *Arthroscopy* 2008; **24**: 113-115 [PMID: 18188873]
- 85 **Lubowitz JH**. Anteromedial portal technique for the anterior cruciate ligament femoral socket: pitfalls and solutions. *Arthroscopy* 2009; **25**: 95-101 [PMID: 19111224 DOI: 10.1016/j.arthro.2008.10.012]
- 86 **Rayan F**, Nanjayan SK, Quah C, Ramoutar D, Konan S, Haddad FS. Review of evolution of tunnel position in anterior cruciate ligament reconstruction. *World J Orthop* 2015; **6**: 252-262 [PMID: 25793165 DOI: 10.5312/wjo.v6.i2.252]
- 87 **Zantop T**, Kubo S, Petersen W, Musahl V, Fu FH. Current techniques in anatomic anterior cruciate ligament reconstruction. *Arthroscopy* 2007; **23**: 938-947 [PMID: 17868832 DOI: 10.1016/j.arthro.2007.04.009]
- 88 **Crawford C**, Nyland J, Landes S, Jackson R, Chang HC, Nawab A, Caborn DN. Anatomic double bundle ACL reconstruction: a literature review. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 946-964; discussion 945 [PMID: 17534599 DOI: 10.1007/s00167-007-0343-7]
- 89 **Zantop T**, Diermann N, Schumacher T, Schanz S, Fu FH, Petersen W. Anatomical and nonanatomical double-bundle anterior cruciate ligament reconstruction: importance of femoral tunnel location on knee kinematics. *Am J Sports Med* 2008; **36**: 678-685 [PMID: 18296542 DOI: 10.1177/0363546508314414]
- 90 **Ho JY**, Gardiner A, Shah V, Steiner ME. Equal kinematics between central anatomic single-bundle and double-bundle anterior cruciate ligament reconstructions. *Arthroscopy* 2009; **25**: 464-472 [PMID: 19409303 DOI: 10.1016/j.arthro.2009.02.013]
- 91 **Bedi A**, Maak T, Musahl V, O'Loughlin P, Choi D, Citak M, Pearle AD. Effect of tunnel position and graft size in single-bundle anterior cruciate ligament reconstruction: an evaluation of time-zero knee stability. *Arthroscopy* 2011; **27**: 1543-1551 [PMID: 21705174 DOI: 10.1016/j.arthro.2011.03.079]
- 92 **Siebold R**. The concept of complete footprint restoration with guidelines for single- and double-bundle ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 699-706 [PMID: 21222101 DOI: 10.1007/s00167-010-1376-x]
- 93 **Chhabra A**, Kline AJ, Nilles KM, Harner CD. Tunnel expansion after anterior cruciate ligament reconstruction with autogenous hamstrings: a comparison of the medial portal and transtibial techniques. *Arthroscopy* 2006; **22**: 1107-1112 [PMID: 17027409 DOI: 10.1016/j.arthro.2006.05.019]
- 94 **Griffith TB**, Allen BJ, Levy BA, Stuart MJ, Dahm DL. Outcomes of repeat revision anterior cruciate ligament reconstruction. *Am J Sports Med* 2013; **41**: 1296-1301 [PMID: 23605223 DOI: 10.1177/0363546513482568]
- 95 **van Eck CF**, Kopf S, Irrgang JJ, Blankevoort L, Bhandari M, Fu FH, Poolman RW. Single-bundle versus double-bundle reconstruction for anterior cruciate ligament rupture: a meta-analysis--does anatomy matter? *Arthroscopy* 2012; **28**: 405-424 [PMID: 22370060 DOI: 10.1016/j.arthro.2011.11.021]
- 96 **Desai N**, Björnsson H, Musahl V, Bhandari M, Petzold M, Fu FH, Samuelsson K. Anatomic single- versus double-bundle ACL reconstruction: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 1009-1023 [PMID: 24343279 DOI: 10.1007/s00167-013-2811-6]
- 97 **Paxton ES**, Kymes SM, Brophy RH. Cost-effectiveness of anterior cruciate ligament reconstruction: a preliminary comparison of single-bundle and double-bundle techniques. *Am J Sports Med* 2010; **38**: 2417-2425 [PMID: 20829416 DOI: 10.1177/0363546510375545]
- 98 **Hofbauer M**, Muller B, Murawski CD, Baraga M, van Eck CF, Fu FH. Strategies for revision surgery after primary double-bundle anterior cruciate ligament (ACL) reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2072-2080 [PMID: 23579225 DOI: 10.1007/s00167-013-2470-7]
- 99 **Herbort M**, Tecklenburg K, Zantop T, Raschke MJ, Hoser C, Schulze M, Petersen W, Fink C. Single-bundle anterior cruciate ligament reconstruction: a biomechanical cadaveric study of a rectangular quadriceps and bone--patellar tendon--bone graft configuration versus a round hamstring graft. *Arthroscopy* 2013; **29**: 1981-1990 [PMID: 24140140 DOI: 10.1016/j.arthro.2013.08.030]
- 100 **Grøntvedt T**, Engebretsen L, Benum P, Fasting O, Mølster A, Strand T. A prospective, randomized study of three operations for acute rupture of the anterior cruciate ligament. Five-year follow-up

- of one hundred and thirty-one patients. *J Bone Joint Surg Am* 1996; **78**: 159-168 [PMID: 8609105]
- 101 **Eggl S**, Kohlhof H, Zumstein M, Henle P, Hartel M, Evangelopoulos DS, Bonel H, Kohl S. Dynamic intraligamentary stabilization: novel technique for preserving the ruptured ACL. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1215-1221 [PMID: 24651979 DOI: 10.1007/s00167-014-2949-x]
- 102 **Kohl S**, Evangelopoulos DS, Ahmad SS, Kohlhof H, Herrmann G, Bonel H, Eggl S. A novel technique, dynamic intraligamentary stabilization creates optimal conditions for primary ACL healing: a preliminary biomechanical study. *Knee* 2014; **21**: 477-480 [PMID: 24405792 DOI: 10.1016/j.knee.2013.11.003]
- 103 **Kohl S**, Stock A, Ahmad SS, Zumstein M, Keel M. Dynamic intraligamentary stabilization and primary repair: A new concept for the treatment of knee dislocation. *Injury* 2015; **46**: 724-728 [DOI: 10.1016/j.injury.2014.10.012]
- 104 **Heitmann M**, Gerau M, Hötzel J, Giannakos A, Frosch KH, Preiss A. [Ligament bracing--augmented primary suture repair in multiligamentous knee injuries]. *Oper Orthop Traumatol* 2014; **26**: 19-29 [PMID: 24553686 DOI: 10.1007/s00064-013-0263-2]

P- Reviewer: Bicanic G, Fukuchi RK, Mugnai R, Seijas R
S- Editor: Gong ZM **L- Editor:** A **E- Editor:** Liu SQ



Direct anterior total hip arthroplasty: Comparative outcomes and contemporary results

Keith P Connolly, Atul F Kamath

Keith P Connolly, Atul F Kamath, Department of Orthopedic Surgery, Center for Hip Preservation, Penn Medicine, University of Pennsylvania, Philadelphia, PA 19107, United States

Author contributions: Connolly KP and Kamath AF contributed to this paper.

Conflict-of-interest statement: The authors have no conflicts of interest to disclose pertaining to the subject of this review manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Atul F Kamath, MD, Department of Orthopedic Surgery, Center for Hip Preservation, Penn Medicine, University of Pennsylvania, 800 Spruce Street, 8th Floor Preston, Philadelphia, PA 19107, United States. akamath@post.harvard.edu
 Telephone: +1-215-6878169
 Fax: +1-215-8292492

Received: May 29, 2015

Peer-review started: June 2, 2015

First decision: September 29, 2015

Revised: October 25, 2015

Accepted: December 3, 2015

Article in press: December 4, 2015

Published online: February 18, 2016

Abstract

Direct anterior total hip arthroplasty has become increasingly more popular among arthroplasty surgeons, in large part due to the use of an intramuscular interval and desire to reduce soft tissue damage. Several studies have now been published comparing the anterior

intramuscular to other commonly used approaches, and many studies have published complication rates on large series of patients. Review of comparative studies indicates direct anterior hips tend towards shorter hospital stays and high rates of patients discharged to home. Although some studies show evidence of early benefit in functional outcomes, there is no strong evidence that the anterior approach provides any long term functional improvements compared to other approaches. Additionally, evidence to support reduced damage to soft tissue may not translate to certain clinical significance. Rates of intra-operative femur fracture, operative time and blood loss rates are notably higher for those developing familiarity with this approach. However, when surgeons have performed a modest number of procedures, the complication rates tend to markedly decrease in most studies to levels comparable to other approaches. Accuracy of component positioning also favors the anterior approach in some studies. This review summarizes the available literature comparing the direct anterior to other approaches for total hip arthroplasty and provides a comprehensive summary of common complications.

Key words: Complications; Direct anterior approach; Surgical hip approaches; Outcomes; Total hip arthroplasty

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Direct anterior total hip arthroplasty may provide higher rates of patients discharged to home and shorter hospital stays when compared to other approaches. Long term functional outcomes do not appear to be improved by an intramuscular approach. Complication rates may be high during the initial learning period of performing this approach; however, these rates are generally shown to not exceed that of other approaches once a surgeon has completed a modest number of cases.

Connolly KP, Kamath AF. Direct anterior total hip arthroplasty: Comparative outcomes and contemporary results. *World J Orthop* 2016; 7(2): 94-101 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/94.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.94>

INTRODUCTION

The continued desire to perform hip reconstruction through less invasive and tissue sparing methods has markedly increased the proliferation of direct anterior total hip arthroplasty (THA) over the past 15 years^[1]. Although an abundance of recent material has been promoted, largely online, to tout the direct anterior approach (DAA) as superior to other commonly performed approaches, strong evidence to support these claims has been lacking^[2]. Several studies seem to indicate that hospital length of stay and percentage of patients discharged home are improved *via* the DAA. These results may be balanced by increased operative time and blood loss, particularly early in the surgeon's performance of this technique. Studies evaluating damage to soft tissues between approaches seem to favor the DAA, yet differences in pain and other patient-reported variables do not consistently show a significant advantage. Functional outcomes tend to be improved in the early post-operative period using the DAA; however, these differences are largely equivalent in longer-term follow-up. Complication rates in this review were consistent with other approaches and appear to be markedly reduced as a surgeon gains familiarity with the procedure.

OUTCOMES AND COMPARATIVE STUDIES

Outcomes related to modern practice of anterior hip arthroplasty have been described in a number of studies, though the vast majority has been retrospective with small or moderate sample sizes. There have been an increasing number of recent prospective studies comparing DAA with other approaches, including less-invasive or minimal-incision posterior and lateral approaches. Results of the only meta-analysis comparing anterior and posterior approaches showed the anterior approach may provide potential benefits in patient reported pain and functional outcomes, post-operative length of stay, dislocations and post-operative narcotic requirements. It further suggested that the anterior approach trended toward higher percentages of patients discharged home and percentages of cups placed within the Lewinnek safe zone^[3].

Several studies have looked at the inpatient and early post-operative outcomes comparing different THA approaches. A comparison of selected outcomes from studies included in this review is summarized in Table 1. Alecci *et al.*^[4] compared 419 patients receiving standard

lateral and minimally invasive direct anterior approaches showing similar operative time and blood loss, with less pain, shorter time to and more patients discharged home with the DAA. A retrospective review of 372 less invasive direct lateral and 258 anterior supine intramuscular anterior approaches showed greater estimated blood loss (EBL), more patients discharged home, higher Harris Hip Scores (HHS), and higher Lower Extremity Activity scores at six weeks in the anterior group. Hospital length of stay and operative time were equal between the two groups^[5]. A comparison by D'Arrigo *et al.*^[6] of three tissue sparing methods (direct anterior, direct lateral and anterolateral) with a standard lateral approach control group, found a decrease in blood loss compared to the control in all groups, better early functional scores in the direct anterior and anterolateral groups, and lower complication rate with an anterolateral approach. There was no difference in hospital stay. Of note, the study groups were comprised of only twenty patients each and were the first tissue sparing surgeries performed by the surgeon for each approach. A retrospective comparison of 100 minimal-incision DAA and 100 transgluteal lateral approaches showed decreased hospital length of stay, decreased pain on post-operative day zero and one, and decreased time to reach defined range of motion for the anterior approach. However, pain during physiotherapy was higher during some time periods for the DA hips^[7]. A retrospective comparison of 41 anterior and 47 posterior approaches found shorter hospital stay and fewer days to mobilization with the anterior approach. Incision length was shorter in the anterior approach; however, lateral femoral cutaneous nerve injury and fracture were more common with the anterior approach and operative time was 20% longer. There was a 56% rate of any complications with the anterior compared to 45% with the posterior approach^[8].

A study comparing DAA and mini-posterior approach performed by two experienced surgeons found no difference in return to activities of daily living (ADLs), length of stay, complication rate, pain medication requirements, physical therapy metrics or discharge disposition. The direct anterior approach had a longer operative time, higher visual analog scale pain score in the hospital, and more patients requiring gait aids at two weeks. Direct anterior hips had higher Harris hip scores at 8 wk; however, fewer patients had returned to work and driving. There were no differences in use of gait aids or narcotics, performance of ADLs, or 0.5 mile walking at 8 wk. The DAA group had lower minor wound complications. Component placement was adequate in both groups^[9]. Spaans compared 46 DA and direct lateral (DL) hips, with operative time and EBL about double with the DA group. The DA hips in the study were the first performed by the surgeons. Hospital stays were equivalent^[10]. A comparison of 54 patient randomized to mini-posterior approach THA (MPA-THA) or DA THA showed time to ambulation without assistive device favored DA-THA (22 d vs 28 d). Three weeks SF-12 mental scores and WOMAC function and total

Table 1 Summary of select outcomes reported in the literature in comparative studies of direct anterior and other total hip approaches

Author	Study variable						
	Length of stay	Discharge to home	Post-operative pain	Short-term functional outcome	Long-term functional outcome	Blood loss	Operative time
Alecci	↓	↑	↓			↔	↔
Barrett	↓		↓	↑	↔	↑	↑
Berend	↔	↑		↑	↔	↑	↔
D'Arrigo	↔			↑	↔	↓	↑
Goebel	↓		↓				
Lamontagne				↔	↔		
Martin	↓	↔		↑	↔	↔	↑
Mayr				↑	↔		
Poehling-monaghan	↔	↔	↑	↔	↔		↑
Rathod				↔	↔		
Rodriguez	↔		↔	↑	↔		
Spaans	↔			↔	↔	↑	↑
Taunton				↑	↔		
Zawadsky	↓	↑	↓	↑			

Arrows indicate relative magnitude of the variable (*i.e.*, ↑: Increased; ↓: Decreased; ↔: Similar) for direct anterior approach compared to alternative approach for applicable study.

scores favored MPA. There were no differences at any other time point for SF-12, WOMAC or HHS scores^[11]. A study of 50 posterior, 50 DA and 50 DA approaches in a learning curve period showed decreased length of stay and more patients discharged to home in the DA groups. The DA groups also had significantly less use of assistive devices, pain scores and narcotic use at six weeks. Operative time for the learning curve group was significantly longer^[12].

Another area of interest in assessing approaches to the hip joint is functional capacity of patient post-operatively. A prospective, randomized, single surgeon study compared 43 direct anterior approaches to 44 posterior approaches, with the primary endpoint of normal ability to climb stairs and walk unlimited distances. The study showed that DAA patients performed better in the immediate post-operative period with lower Visual Analog Scale pain scores on post-operative day one, more subjects climbing stairs and walking unlimited distances at six weeks and higher HOOS Symptoms scores at three months. However, there were no significant differences at later time points^[13]. A comparison of 60 hips between anterior muscle-sparing, direct lateral approaches and a matched control group showed abnormal stair climbing kinematics were exhibited in both groups after surgery. There were fewer differences with smaller magnitudes when compared to the control population in the anterior group than the lateral group^[14]. A gait analysis study by Mayr *et al*^[15] compared sixteen direct anterior hips and seventeen anterolateral hips. At six and twelve weeks, the anterior hip group showed significant improvement in cadence, stride length and time and walking speed. The anterolateral group showed no statistically significant improvements in time-distance parameters at six or twelve weeks. Normal level of walking speed was not achieved in either group. Both groups showed

improvements in range of motion; however, neither group achieved a physiologically normal range of flexion/extension in the study period. A comparison of gait parameters in 22 patients, 11 direct anterior and 11 posterior approaches, showed improvements in flexion/extension range of motion, peak flexion, and extension moments without differences between the groups. The DAA group showed statistically significant improvements in external and internal rotation compared to the posterior group, which may be related to release and repair of external rotators in posterior group. The posterior approach group had a significant improvement in gait velocity from pre-operatively to 6 mo, becoming similar to the pre-op value for DAA^[16].

A comparison of 35 computer-navigated minimally-invasive anterior approach and 40 posterolateral approach hips found no differences in recovery of spatiotemporal parameters or angular movements of the pelvis and thorax between the groups. Both groups retained lower values for spatiotemporal parameters and frontal plane angular movements compared to healthy subjects at six months and one year^[17].

A prospective non-randomized trial comparing 60 DAA and 60 posterior hips showed early functional differences favoring the DAA group, including improved timed up and go (TUG) parameters immediately post-operatively, faster time to walk 150 feet and stairs and transfers. Beyond two weeks, there were no differences in HHS, University of California at Los Angeles (UCLA), functional independence measure (M-FIM), and TUG scores, as well as need for gait aids, time to walk 0.5 miles or resumption of activities of daily living^[18]. An analysis of 20 DAA and 20 direct lateral hips compared to 20 controls showed negligible difference between the two approach groups with both groups showing gait anomalies. Neither group achieved kinetics and kinematics similar to the control group^[19]. A small study

comparing DAA and anterolateral THAs with a control group showed no difference in return of hip strength and mobility between the two groups compared to control groups. Patients in the DAA hip group showed greater gait velocity and stride length, abductor strength and sagittal plane range of motion at six weeks compared to pre-operatively, but was not significantly different in improvement from the anterolateral group. Strength and mobility between DAA and anterolateral groups were similar at 16 wk post-surgery^[20].

A limited number of studies have also evaluated the patients' perceived outcomes related to the surgical approach. A survey of 1273 patients in approximately equal distribution of lateral, anterior and posterolateral approach groups showed that adjusted HOOS scores for pain, other symptoms, activities of daily living, sport/recreation, and quality of life (QOL) were significantly worse for the lateral approach than for the anterior approach and the posterolateral approach. These results were largely related to more patient-reported limping with the lateral approach than with the anterior and posterolateral^[21]. A prospective, randomized comparison of 100 patients enrolled in either a modified direct anterior or small-incision anterolateral approach of equivalent incision lengths showed better improvement in SF-36 scores for role limitation, bodily pain and general mental health for patients in the anterior group^[22]. A comparison of 85 DAA hips and 86 transgluteal lateral hips found no difference in HHS, SF-36 mental and physical component scores and daily activity by daily activity questionnaire. There was a significant difference in the UCLA activity score, with the lateral group scoring higher^[23]. A prospective randomized trial between 50 DAA and 50 DL hips showed improvements at follow-up up to one year that were statistically significantly better for DAA in physical functioning, role limitations, bodily pain, social functioning, general mental health, vitality energy or fatigue and post-op physical and mental health dimensions of the SF-36, WOMAC and QOL component of Linear Analogy Scale Assessment. There were no differences remaining at 2 years^[24].

One of the main arguments for superiority of the DAA is the minimal soft tissue and muscle damage resulting from utilizing an intramuscular plane. Twenty-nine patients treated with minimally invasive THA through a DAA and twenty-eight patients treated with the same procedure through a posterior approach were prospectively analyzed. The levels of the markers of inflammation were slightly decreased in the direct-anterior-approach group as compared with those in the posterior-approach group. The rise in the CK level in the posterior-approach group was 5.5 times higher than that in the anterior-approach group in the post-anesthesia-care unit and nearly twice as high cumulatively^[25]. A study comparing 25 DAA and transgluteal approaches found detachment of abductor insertion, partial tears and tendinosis of the glut medius and minimus, presence of peri-trochanteric bursal fluid and gluteus medius and minimus fatty atrophy were significantly less in DAA

approach when compared using magnetic resonance imaging one year post-operatively^[26]. A comparison of visually inspected muscle damage to cadaveric specimens undergoing anterior or posterior approaches showed less damage to the gluteus medius and minimus with the anterior approach. Thirty-one percent of the anterior hips showed evidence of tensor fascia lata (TFL) damage and 12% had damage to the direct head of the rectus femoris. The greatest difference was in damage to the gluteus minimus. All external rotators were released as part of the posterior approach, whereas 50% of anterior hip procedures required release for mobilization^[27]. A study of 421 DAA hips estimated that increasing TFL damage was related to the male sex and increasing body mass index (BMI)^[28]. The incidence of heterotopic ossification (HO), possibly related to retraction damage to the TFL or rectus femoris, has also been evaluated in anterior hips. An analysis of 236 hips in 214 patients at two hospitals undergoing DAA showed an overall incidence of HO of 41.5% between two hospitals. There was a significant reduction in patients on aspirin compared to Coumadin or Lovenox for deep venous thrombosis prophylaxis, and a higher rate in male patients. Hospital One had an incidence of 33% compared to 48.8% at Hospital Two. The rate of HO was similar to reported rates of 28%-61% with other approaches. It was hypothesized that use of the OSI Hana table and mechanical lift at Hospital One may have reduced soft tissue trauma and also contributed to lower HO rates^[29].

In summary, several studies seem to indicate that hospital length of stay and percentage of patients discharged to home are improved *via* the DAA. These results may be balanced by increased operative time and blood loss, particularly early in the surgeon's performance of this technique. Some functional outcomes may be improved in the early post-operative period using the DAA; however, these results are largely negligible in long-term follow-up.

COMPLICATIONS

One of the common arguments against the DAA is the high rate of complications. Table 2 summarizes reported complications from multiple studies and available complications from comparative approaches. Several studies note markedly higher rates of complications in the "learning curve" period, or the initial series of surgeries performed by a surgeon adapting the approach. Moskal *et al*^[30] proposed that the surgeons level of experience with DA approach directly correlated with complication rates, with a plateau between the first 40-100 cases. A study reporting outcomes of the first 43 cases performed by a single surgeon showed significant reductions in operative time and EBL between the first and last ten cases performed, with a decline in total complications^[31]. Seng *et al*^[32] tracked conversion of surgeries from lateral to DAA, and found that after 6 mo and 37 cases, more than half of joint replacements were being performed

Table 2 Summary of select complications reported in the literature in comparative studies of direct anterior and other total hip approaches n (%)

Author	Approach	No. patients	Complications													
			Dislocation	Femur fracture	Great trochanter fracture	Hematoma	Ankle injury	Nerve injury	Reoperation due to infection	Reoperation - other than infection	Bursitis	Superficial infection/wound complication	Acetabulum (or pelvis) fracture			
Alexandrov	A	43	1 (2.3)	1 (2.3)	5 (11.6)	1 (2.3)	0	2 (4.7)								
Amile	A	421	13 (3.1)					25 (5.9)	5 (1.2)	8 (1.9)						
	L	431	16 (3.7)					27 (6.3)	8 (1.9)	21 (4.9)						
	P	421	10 (2.4)					14 (3.3)	5 (1.2)	7 (1.7)						
Bal	A	100		1 (1.0)				4 (4.0)								
Barrett	A	43	0 (0.0)	0 (0.0)		1 (2.3)								1 (2.3)		
	P	44	1 (2.3)	1 (2.3)		0 (0.0)								0 (0.0)		
Berend	A	258		4 (1.6)												
	L	375				2 (0.5)		2 (0.8)	1 (0.3)	2 (0.5)				1 (0.3)		1 (0.3)
Bhandari	A	1277	8 (0.6)	22 (1.7)	13 (1.0)	5 (0.4)		13 (1.0)	3 (0.2)	32 (2.5)	1 (0.1)			22 (1.7)		8 (0.6)
Christensen	A	505							3 (0.6)	2 (0.4)				2 (0.4)		
	P	1288							1 (0.1)	1 (0.1)						
De Geest	A	300	2 (0.7)	12 (4.0)	3 (1.0)			16 (5.3)	6 (2.0)	14 (4.7)				6 (2.0)		
Hallert	A	200	4 (2.0)	3 (2.0)				3 (2.0)	1 (1.0)							
Hoell	A	113	0 (0.0)	1 (0.9)					1 (0.9)	3 (2.7)						
Keggi	A	687	17 (2.5)	15 (2.2)	5 (0.7)	13 (1.9)		5 (0.7)	1 (0.1)							
Jewett	A	800	7 (0.9)	24 (3.0)	0 (0.0)			1 (0.1)	7 (0.9)	19 (2.4)						1 (0.1)
Kennon	A	2222	28 (1.3)	63 (2.8)	24 (1.1)	31 (1.4)		9 (0.4)	7 (0.3)					3 (7.3)		3 (0.1)
Martin	A	41	1 (2.4)	1 (2.4)				7 (17.1)	1 (0.2)					4 (8.5)		
	P	47	3 (6.4)	0 (0.0)	3 (0.6)	3 (0.6)		0 (0.0)	1 (0.4)							
Matta	A	494	3 (0.6)	6 (1.2)					1 (0.2)	3 (0.6)						
Mirza	A	258	4 (1.5)	9 (3.5)					1 (0.4)							
Reichert	A	85	0 (0.0)	1 (1.2)				6 (7.1)								
	L	86	0 (0.0)	1 (1.2)					1 (1.2)	1 (1.2)						
Sariali	A	1764	27 (1.5)	28 (1.6)	1 (0.1)											
Spaans	A	46	1 (2.2)													
	P	46	1 (2.2)													
Wayne	A	100	2 (2.0)	8 (8.0)				6 (6.0)	0 (0.0)	5 (5.0)				0 (0.0)		1 (2.2)
	L	100	1 (1.0)	2 (2.0)				0 (0.0)	3 (3.0)	3 (3.0)				4 (4.0)		3 (3.0)
Yi	A	61	1 (1.6)	2 (3.3)	3 (4.9)	1 (1.6)		1 (1.6)	1 (1.6)	2 (3.3)						1 (1.0)
Zawadsky	A	100	0 (0.0)						2 (2.0)	3 (3.0)						
	P	50	1 (2.0)					3 (6.0)	3 (6.0)	0 (0.0)						

A: Anterior; L: Lateral; P: Posterior.

with the anterior approach, indicating increased comfort with the procedure. This time mark also coincided with a plateau in operative time and EBL. They had two femoral perforations during this learning curve period and observed no dislocations. Surgeons who performed less than 100 cases had a twofold increase in complications in one review of 1277 DAA THAs^[33]. Wayne *et al*^[34] compared the first 100 patients in a DAA compared to the previous 100 patients receiving a direct lateral approach and showed increased blood loss (change in hemoglobin pre- vs post-operatively), longer operative time, increased rate of nerve damage, femur fracture, blood transfusion, acetabular malposition, with shorter hospital stays and fewer operative site infections.

Femur fractures have been particularly found to be of high incidence in initial adaptation of the approach. A study of 800 DA hips showed a significantly higher rate

of femur fracture early in the series, with none in the second half. A second-generation fracture table with electronic hook elevation system, allowing for more gradual and gentle femoral elevation, was attributed to reduce the rate of fracture, along with better understanding of tension applied to the femur and necessary superior capsule and occasional piriformis tendon release during exposure. Femoral perforations also occurred early in the series in patients with severe flexion contracture which was mitigated through better understanding of the using a more horizontal insertion angle of starting broach to follow the angle of the femur in the contracted position^[35]. Yi *et al.*^[36] reported an 8.2% rate of intraoperative femoral fracture during the first 61 cases of anterior supine intermuscular THA performed, all occurring during the first 32 of 61 cases. De Geest *et al.*^[37] compared early outcomes and complications of 300 hips and showed 5 proximal femur fractures with Medacta Quadra and anterior minimally invasive surgery stems but none in the group using Taperloc stems. They did not find a difference in infection rates between early and later cases, but had a high rate of post-operative overall complication rate (14%), and 6.7% of patients required a surgical re-intervention. The authors concluded that there may be a significant learning curve with a complication rate that may be too high for some surgeons to change their surgical technique.

Dislocation rates have been shown to be low with the DAA in several studies. It is postulated that inherent stability exists, as muscles are not detached posteriorly or anteriorly^[38]. Siguier showed a dislocation rate of 0.96% (10 of 1037 patients) with MIS DAA THA^[39]. An analysis of 22237 hips performed through posterior, anterolateral, direct lateral, and anterior approaches found that anterolateral and anterior hips had lower dislocation rates compared to posterior. Among 42438 hips analyzed for need for revision, there was no difference between approaches. The dislocation rate for DA hips was 0.8%^[40]. A prospective study by Sariali *et al.*^[41] of 1764 DA hips found an overall dislocation rate of 1.5%. Significant risk factors for dislocation were male sex, higher BMI, osteonecrosis, head diameter (22 > 28 mm, 2% vs 0.5%), higher EBL and low post-operative range of motion.

Wound complications have also been a source of concern, particularly in obese patients with poorer proximal skin where the DAA incision may lie in the overhanging fat apron or over fold itself. Use of an abdominal binder for patients with pendulous abdomens to keep the pannus from resting on the incision until healed has been suggested, as well as maintaining a sterile bandage^[30]. A comparison of 1288 posterior approach and 505 DAA hips showed a higher rate of re-operation for wound-related complications (0.2% to 1.4%, respectively)^[42]. Some authors have endorsed use of tissue protectors intra-operatively to reduce skin damage; however, use of a ring retractor did not improve wound cosmesis in a small study on the subject^[31,43,44].

CONCLUSION

All standard approaches to the hip have been shown to be safe and efficacious, with particular advantages and disadvantages to each approach. The DAA to the hip has gained significant popularity recently, and can be a valuable technique for hip replacement in most patients. Although it has been associated with a steep learning curve, overall complication rates in the available literature do not appear to exceed those of other approaches to the hip. The growing desire for less invasive arthroplasty with improvement in functional results makes this approach an attractive choice. The surgeon must carefully consider the possible benefits and disadvantages of the approach, especially in an early phase of adopting the procedure. Long-term studies of larger numbers of patients are still required to demonstrate a cost benefit or quality of care advantage to other hip approaches. As patient driven health care and hospital associated costs became a larger factor in the practice of arthroplasty, the trends in outcomes related to direct anterior total hip arthroplasty should be more closely examined.

REFERENCES

- 1 **Post ZD**, Orozco F, Diaz-Ledezma C, Hozack WJ, Ong A. Direct Anterior Approach for Total Hip Arthroplasty: Indications, Technique, and Results. *J Am Acad Orthop Surg* 2014; **22**: 595-603 [PMID: 25157041 DOI: 10.5435/JAAOS-22-09-595]
- 2 **Mohan R**, Yi PH, Hansen EN. Evaluating online information regarding the direct anterior approach for total hip arthroplasty. *J Arthroplasty* 2015; **30**: 803-807 [PMID: 25697892 DOI: 10.1016/j.arth.2014.12.022]
- 3 **Higgins BT**, Barlow DR, Heagerty NE, Lin TJ. Anterior vs. posterior approach for total hip arthroplasty, a systematic review and meta-analysis. *J Arthroplasty* 2015; **30**: 419-434 [PMID: 25453632 DOI: 10.1016/j.arth.2014.10.020]
- 4 **Alecci V**, Valente M, Crucil M, Minerva M, Pellegrino CM, Sabbadini DD. Comparison of primary total hip replacements performed with a direct anterior approach versus the standard lateral approach: perioperative findings. *J Orthop Traumatol* 2011; **12**: 123-129 [PMID: 21748384 DOI: 10.1007/s10195-011-0144-0]
- 5 **Berend KR**, Lombardi AV, Seng BE, Adams JB. Enhanced early outcomes with the anterior supine intermuscular approach in primary total hip arthroplasty. *J Bone Joint Surg Am* 2009; **91** Suppl 6: 107-120 [PMID: 19884418 DOI: 10.2106/JBJS.I.00525]
- 6 **D'Arrigo C**, Speranza A, Monaco E, Carcangiu A, Ferretti A. Learning curve in tissue sparing total hip replacement: comparison between different approaches. *J Orthop Traumatol* 2009; **10**: 47-54 [PMID: 19384637 DOI: 10.1007/s10195-008-0043-1]
- 7 **Goebel S**, Steinert AF, Schillinger J, Eulert J, Broscheit J, Rudert M, Nöth U. Reduced postoperative pain in total hip arthroplasty after minimal-invasive anterior approach. *Int Orthop* 2012; **36**: 491-498 [PMID: 21611823 DOI: 10.1007/s00264-011-1280-0]
- 8 **Martin CT**, Pugely AJ, Gao Y, Clark CR. A comparison of hospital length of stay and short-term morbidity between the anterior and the posterior approaches to total hip arthroplasty. *J Arthroplasty* 2013; **28**: 849-854 [PMID: 23489731 DOI: 10.1016/j.arth.2012.10.029]
- 9 **Poehling-Monaghan KL**, Kamath AF, Taunton MJ, Pagnano MW. Direct anterior versus minimiposterior THA with the same advanced perioperative protocols: surprising early clinical results. *Clin Orthop Relat Res* 2015; **473**: 623-631 [PMID: 25082624 DOI: 10.1007/s11999-014-3827-z]

- 10 **Spaans AJ**, van den Hout JA, Bolder SB. High complication rate in the early experience of minimally invasive total hip arthroplasty by the direct anterior approach. *Acta Orthop* 2012; **83**: 342-346 [PMID: 22880711 DOI: 10.3109/17453674.2012.711701]
- 11 **Taunton MJ**, Mason JB, Odum SM, Springer BD. Direct anterior total hip arthroplasty yields more rapid voluntary cessation of all walking aids: a prospective, randomized clinical trial. *J Arthroplasty* 2014; **29**: 169-172 [PMID: 25007723 DOI: 10.1016/j.arth.2014.03.051]
- 12 **Zawadsky MW**, Paulus MC, Murray PJ, Johansen MA. Early outcome comparison between the direct anterior approach and the mini-incision posterior approach for primary total hip arthroplasty: 150 consecutive cases. *J Arthroplasty* 2014; **29**: 1256-1260 [PMID: 24405626 DOI: 10.1016/j.arth.2013.11.013]
- 13 **Barrett WP**, Turner SE, Leopold JP. Prospective randomized study of direct anterior vs postero-lateral approach for total hip arthroplasty. *J Arthroplasty* 2013; **28**: 1634-1638 [PMID: 23523485 DOI: 10.1016/j.arth.2013.01.034]
- 14 **Lamontagne M**, Varin D, Beaulé PE. Does the anterior approach for total hip arthroplasty better restore stair climbing gait mechanics? *J Orthop Res* 2011; **29**: 1412-1417 [PMID: 21437967 DOI: 10.1002/jor.21392]
- 15 **Mayr E**, Nogler M, Benedetti MG, Kessler O, Reinthaler A, Krismer M, Leardini A. A prospective randomized assessment of earlier functional recovery in THA patients treated by minimally invasive direct anterior approach: a gait analysis study. *Clin Biomech* (Bristol, Avon) 2009; **24**: 812-818 [PMID: 19699566 DOI: 10.1016/j.clinbiomech.2009.07.010]
- 16 **Rathod PA**, Orishimo KF, Kremenic IJ, Deshmukh AJ, Rodriguez JA. Similar improvement in gait parameters following direct anterior & posterior approach total hip arthroplasty. *J Arthroplasty* 2014; **29**: 1261-1264 [PMID: 24405621 DOI: 10.1016/j.arth.2013.11.021]
- 17 **Reininga IH**, Stevens M, Wagenmakers R, Boerboom AL, Groothoff JW, Bulstra SK, Zijlstra W. Comparison of gait in patients following a computer-navigated minimally invasive anterior approach and a conventional posterolateral approach for total hip arthroplasty: a randomized controlled trial. *J Orthop Res* 2013; **31**: 288-294 [PMID: 22886805 DOI: 10.1002/jor.22210]
- 18 **Rodriguez JA**, Deshmukh AJ, Rathod PA, Greiz ML, Deshmane PP, Hepinstall MS, Ranawat AS. Does the direct anterior approach in THA offer faster rehabilitation and comparable safety to the posterior approach? *Clin Orthop Relat Res* 2014; **472**: 455-463 [PMID: 23963704 DOI: 10.1007/s11999-013-3231-0]
- 19 **Varin D**, Lamontagne M, Beaulé PE. Does the anterior approach for THA provide closer-to-normal lower-limb motion? *J Arthroplasty* 2013; **28**: 1401-1407 [PMID: 23507070 DOI: 10.1016/j.arth.2012.11.018]
- 20 **Klausmeier V**, Lugade V, Jewett BA, Collis DK, Chou LS. Is there faster recovery with an anterior or anterolateral THA? A pilot study. *Clin Orthop Relat Res* 2010; **468**: 533-541 [PMID: 19763725 DOI: 10.1007/s11999-009-1075-4]
- 21 **Amlie E**, Havelin LI, Furnes O, Baste V, Nordsletten L, Hovik O, Dimmen S. Worse patient-reported outcome after lateral approach than after anterior and posterolateral approach in primary hip arthroplasty. A cross-sectional questionnaire study of 1,476 patients 1-3 years after surgery. *Acta Orthop* 2014; **85**: 463-469 [PMID: 24954494 DOI: 10.3109/17453674.2014.934183]
- 22 **Bender B**, Nogler M, Hozack WJ. Direct anterior approach for total hip arthroplasty. *Orthop Clin North Am* 2009; **40**: 321-328 [PMID: 19576399 DOI: 10.1016/j.ocl.2009.01.003]
- 23 **Reichert JC**, Volkmann MR, Koppmair M, Rackwitz L, Lüdemann M, Rudert M, Nöth U. Comparative retrospective study of the direct anterior and transgluteal approaches for primary total hip arthroplasty. *Int Orthop* 2015; **39**: 2309-2313 [PMID: 25795247 DOI: 10.1007/s00264-015-2732-8]
- 24 **Restrepo C**, Parvizi J, Pour AE, Hozack WJ. Prospective randomized study of two surgical approaches for total hip arthroplasty. *J Arthroplasty* 2010; **25**: 671-679.e1 [PMID: 20378307 DOI: 10.1016/j.arth.2010.02.002]
- 25 **Bergin PF**, Doppelt JD, Kephart CJ, Benke MT, Graeter JH, Holmes AS, Haleem-Smith H, Tuan RS, Unger AS. Comparison of minimally invasive direct anterior versus posterior total hip arthroplasty based on inflammation and muscle damage markers. *J Bone Joint Surg Am* 2011; **93**: 1392-1398 [PMID: 21915544 DOI: 10.2106/JBJS.J.00557]
- 26 **Bremer AK**, Kalberer F, Pfirrmann CW, Dora C. Soft-tissue changes in hip abductor muscles and tendons after total hip replacement: comparison between the direct anterior and the transgluteal approaches. *J Bone Joint Surg Br* 2011; **93**: 886-889 [PMID: 21705558 DOI: 10.1302/0301-620X.93B7.25058]
- 27 **Meneghini RM**, Pagnano MW, Trousdale RT, Hozack WJ. Muscle damage during MIS total hip arthroplasty: Smith-Petersen versus posterior approach. *Clin Orthop Relat Res* 2006; **453**: 293-298 [PMID: 17006366 DOI: 10.1097/01.blo.0000238859.46615.34]
- 28 **Frye BM**, Berend KR, Lombardi AV, Morris MJ, Adams JB. Do sex and BMI predict or does stem design prevent muscle damage in anterior supine minimally invasive THA? *Clin Orthop Relat Res* 2015; **473**: 632-638 [PMID: 25337974 DOI: 10.1007/s11999-014-3991-1]
- 29 **Tippets DM**, Zaryanov AV, Burke WV, Patel PD, Suarez JC, Ely EE, Figueroa NM. Incidence of heterotopic ossification in direct anterior total hip arthroplasty: a retrospective radiographic review. *J Arthroplasty* 2014; **29**: 1835-1838 [PMID: 24957801 DOI: 10.1016/j.arth.2014.04.027]
- 30 **Moskal JT**, Capps SG, Scanelli JA. Anterior muscle sparing approach for total hip arthroplasty. *World J Orthop* 2013; **4**: 12-18 [PMID: 23362470 DOI: 10.5312/wjo.v4.i1.12]
- 31 **Alexandrov T**, Ahlmann ER, Menendez LR. Early clinical and radiographic results of minimally invasive anterior approach hip arthroplasty. *Adv Orthop* 2014; **2014**: 954208 [PMID: 24715984 DOI: 10.1155/2014/954208]
- 32 **Seng BE**, Berend KR, Ajluni AF, Lombardi AV. Anterior-supine minimally invasive total hip arthroplasty: defining the learning curve. *Orthop Clin North Am* 2009; **40**: 343-350 [PMID: 19576401 DOI: 10.1016/j.ocl.2009.01.002]
- 33 **Bhandari M**, Matta JM, Dodgin D, Clark C, Kregor P, Bradley G, Little L. Outcomes following the single-incision anterior approach to total hip arthroplasty: a multicenter observational study. *Orthop Clin North Am* 2009; **40**: 329-342 [PMID: 19576400 DOI: 10.1016/j.ocl.2009.03.001]
- 34 **Wayne N**, Stoewe R. Primary total hip arthroplasty: a comparison of the lateral Hardinge approach to an anterior mini-invasive approach. *Orthop Rev* (Pavia) 2009; **1**: e27 [PMID: 21808689 DOI: 10.4081/or.2009.e27]
- 35 **Jewett BA**, Collis DK. High complication rate with anterior total hip arthroplasties on a fracture table. *Clin Orthop Relat Res* 2011; **469**: 503-507 [PMID: 20886324 DOI: 10.1007/s11999-010-1568-1]
- 36 **Yi C**, Agudelo JF, Dayton MR, Morgan SJ. Early complications of anterior supine intermuscular total hip arthroplasty. *Orthopedics* 2013; **36**: e276-e281 [PMID: 23464946 DOI: 10.3928/01477447-20130222-14]
- 37 **De Geest T**, Vansintjan P, De Loore G. Direct anterior total hip arthroplasty: complications and early outcome in a series of 300 cases. *Acta Orthop Belg* 2013; **79**: 166-173 [PMID: 23821968]
- 38 **Barton C**, Kim PR. Complications of the direct anterior approach for total hip arthroplasty. *Orthop Clin North Am* 2009; **40**: 371-375 [PMID: 19576405 DOI: 10.1016/j.ocl.2009.04.004]
- 39 **Siguiet T**, Siguiet M, Brumpt B. Mini-incision anterior approach does not increase dislocation rate: a study of 1037 total hip replacements. *Clin Orthop Relat Res* 2004; **(426)**: 164-173 [PMID: 15346069]
- 40 **Sheth D**, Cafri G, Inacio MC, Paxton EW, Namba RS. Anterior and Anterolateral Approaches for THA Are Associated With Lower Dislocation Risk Without Higher Revision Risk. *Clin Orthop Relat Res* 2015; **473**: 3401-3408 [PMID: 25762014 DOI: 10.1007/s11999-015-4230-0]
- 41 **Sariali E**, Leonard P, Mamoudy P. Dislocation after total hip arthroplasty using Hueter anterior approach. *J Arthroplasty* 2008; **23**: 266-272 [PMID: 18280423]
- 42 **Christensen CP**, Karthikeyan T, Jacobs CA. Greater prevalence

of wound complications requiring reoperation with direct anterior approach total hip arthroplasty. *J Arthroplasty* 2014; **29**: 1839-1841 [PMID: 24890998 DOI: 10.1016/j.arth.2014.04.036]

- 43 **Alvarez-Pinzon AM**, Mutnal A, Suarez JC, Jack M, Friedman D, Barsoum WK, Patel PD. Evaluation of wound healing after direct anterior total hip arthroplasty with use of a novel retraction

device. *Am J Orthop* (Belle Mead NJ) 2015; **44**: E17-E24 [PMID: 25566560]

- 44 **Horne PH**, Olson SA. Direct anterior approach for total hip arthroplasty using the fracture table. *Curr Rev Musculoskelet Med* 2011; **4**: 139-145 [PMID: 21713379 DOI: 10.1007/s12178-011-9087-6]

P- Reviewer: Aprato A, Buttaro MA, Cui QT **S- Editor:** Qiu S

L- Editor: A **E- Editor:** Liu SQ



Osteochondritis dissecans of the capitellum in adolescents

Christiaan JA van Bergen, Kimberly IM van den Ende, Bart ten Brinke, Denise Eygendaal

Christiaan JA van Bergen, Department of Orthopedic Surgery, Academic Medical Center, 1105 AZ Amsterdam, The Netherlands

Kimberly IM van den Ende, Bart ten Brinke, Denise Eygendaal, Department of Orthopedic Surgery, Amphia Hospital, 4818 CK Breda, The Netherlands

Author contributions: van Bergen CJA drafted and finalized the manuscript; van den Ende KIM and ten Brinke B provided the figures; Eygendaal D supervised the writing process; all authors reviewed and commented on the text and approved the final version.

Conflict-of-interest statement: The authors have no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Christiaan JA van Bergen, MD, PhD, Department of Orthopedic Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. c.j.vanbergen@amc.nl
Telephone: +31-20-5669111
Fax: +31-20-5669117

Received: May 28, 2015

Peer-review started: June 1, 2015

First decision: August 4, 2015

Revised: September 16, 2015

Accepted: December 1, 2015

Article in press: December 2, 2015

Published online: February 18, 2016

Abstract

Osteochondritis dissecans (OCD) is a disorder of articular cartilage and subchondral bone. In the elbow,

an OCD is localized most commonly at the humeral capitellum. Teenagers engaged in sports that involve repetitive stress on the elbow are at risk. A high index of suspicion is warranted to prevent delay in the diagnosis. Plain radiographs may disclose the lesion but computed tomography and magnetic resonance imaging are more accurate in the detection of OCD. To determine the best treatment option it is important to differentiate between stable and unstable OCD lesions. Stable lesions can be initially treated nonoperatively with elbow rest or activity modification and physical therapy. Unstable lesions and stable lesions not responding to conservative therapy require a surgical approach. Arthroscopic debridement and microfracturing has become the standard initial procedure for treatment of capitellar OCD. Numerous other surgical options have been reported, including internal fixation of large fragments and osteochondral autograft transfer. The aim of this article is to provide a current concepts review of the etiology, clinical presentation, diagnosis, treatment, and outcomes of elbow OCD.

Key words: Osteochondritis dissecans; Cartilage; Elbow; Capitellum; Athletes; Overhead sports; Arthroscopy; Bone marrow stimulation; Adolescent; Osteoarthritis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The aim of this article is to provide a current concepts review of the etiology, clinical presentation, diagnosis, treatment, and outcomes of elbow osteochondritis dissecans. This well illustrated paper highlights the need for a high index of suspicion to prevent delay in the diagnosis. Various imaging methods are outlined. Current treatment options are discussed and future directions are provided.

van Bergen CJA, van den Ende KIM, ten Brinke B, Eygendaal D. Osteochondritis dissecans of the capitellum in adolescents. *World J Orthop* 2016; 7(2): 102-108 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/102.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.102>

INTRODUCTION

Osteochondritis dissecans (OCD) is a process in which a segment of articular cartilage separates from the subchondral bone. In the human body, OCD lesions are most commonly found in the knee, followed by the ankle and the elbow^[1]. OCD of the elbow typically affects the capitellum of the humerus. It can be a debilitating injury in a young patient population.

Epidemiology

Elbow OCD presents typically in adolescent athletes engaged in repetitive overhead or upper extremity weight-bearing activities (*e.g.*, baseball, tennis, volleyball, weight lifting and gymnastics). The prevalence of OCD of the humeral capitellum was 3.4% among more than 2000 adolescent baseball players^[2]. Not all of these patients had symptoms^[2]. Patients with an OCD usually are in their second decade of life, with an age ranging from 11 to 23 years. Boys are affected more commonly than girls. The capitellum of the dominant elbow is mostly affected. Bilateral involvement is seen in up to 20% of the patients^[3].

Elbow OCD should be distinguished from Panner's disease or osteochondrosis of the capitellum. Panner's disease is encountered in younger children (aged 4-12 years), and characterized by ischemia and necrosis of the capitellar epiphysis, followed by regeneration and recalcification. It is a self-limiting, benign disorder that usually resolves with rest.

Etiology

The exact etiology of OCD is unknown. A genetic predisposition has been suggested in twin studies^[4]. The main cause, however, is thought to be excessive repetitive valgus compression across the elbow joint with immature articular cartilage^[5,6]. Repetitive stress to the lateral elbow compartment could lead to localized injury of subchondral bone of the poorly vascularized humeral capitellum (Figure 1), characterized by focal avascular necrosis and subchondral bone changes. Subsequently, this could result in loss of support for the overlying articular cartilage and eventually breakdown and formation of loose fragments once the mechanical support of the articular cartilage is compromised^[5,6].

Pathology

OCD usually evolves through three stages^[3,6]. In stage 1, hyperemic bone and edematous periarticular soft tissues are found. In stage 2, the epiphysis deforms, sometimes with fragmentation. In stage 3, necrotic bone is replaced by granulation tissue. The articular surface may separate and form a loose body as the bone heals.

Natural history

It seems logical to assume that patients with OCD are predisposed to early osteoarthritis of the elbow. However, the relation between cartilage defects in general and the development of osteoarthritis in the long

term has not been elucidated to date. Most evidence is available for cartilage lesions in the knee and ankle^[7,8]. Large chondral and osteochondral lesions of the knee are presumed to predispose to osteoarthritis, although the scientific evidence is limited^[7]. In the ankle, however, a relation between OCD and osteoarthritis has not been shown^[8]. Only 4% of ankle OCDs develop a narrowed joint space up to 20 years of follow-up^[9].

With regard to the elbow, little is known about the risk of developing degenerative changes in the long term. Bauer *et al.*^[10] investigated elbow degeneration amongst 31 OCD patients at a mean follow-up of 23 years. One-third had radiographic degenerative changes and 42% of patients complained of pain and/or reduced range of motion at the time of follow-up. Younger patients had better odds of having a pain-free elbow without radiographic signs of degeneration in the long term. In addition, larger lesions may be more prone to degenerative changes over time. Takahara *et al.*^[11] noted a poorer long-term outcome of patients with large cartilage lesions compared to those with small lesions. There is no evidence that surgical debridement with or without microfracturing protects against degeneration.

CLINICAL PRESENTATION

Patient's delay and doctor's delay are very common in elbow OCD. Therefore, a high index of suspicion and directed imaging studies are necessary. In fact, any teenager presenting with lateral elbow pain should be suspected of having an OCD lesion. The typical patient is a young male sports person, initially presenting with pain, tenderness, and swelling over the lateral aspect of the elbow^[12]. In a later stage, there may be loss of extension and intermittent catching and locking of the elbow, but physical examination findings are not very distinct in the early stage of OCD. Yet, it is important to detect OCD as early as possible to prevent expansion of the lesion and possible degeneration of the joint.

IMAGING

Plain anteroposterior and lateral radiographs are often used as an initial screening method (Figure 2). Radiographic signs of an OCD are flattening of the capitellum, a focal defect of the articular surface, and loose bodies. However, routine radiographs of the elbow are insensitive in identifying OCD of the capitellum^[13]. In fact, approximately half of the radiographs of patients with a capitellar OCD appear normal^[13]. An anteroposterior view with the elbow in 45° of flexion may better depict the lesion^[14].

Because of the low sensitivity of plain radiography, additional imaging is indicated when an OCD is suspected. Ultrasound of the elbow has been described to detect capitellar OCD^[15-17]. However, the capitellum is partially obscured by the radial head^[17]. Computed tomography (CT) and magnetic resonance imaging (MRI) are most useful in diagnosing an OCD. MRI demonstrates

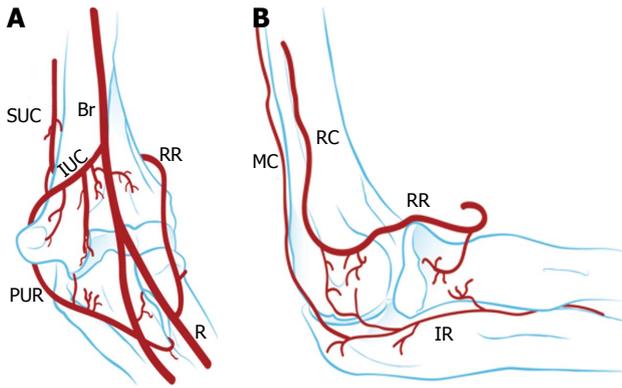


Figure 1 Vascularisation of the capitellum. A: Anterior view; B: Lateral view. Br: Brachial; IR: Interosseous recurrent; IUC: Inferior ulnar collateral; MC: Middle collateral; PUR: Posterior ulnar recurrent; R: Radial; RC: Radial collateral; RR: Radial recurrent; SUC: Superior ulnar collateral artery.

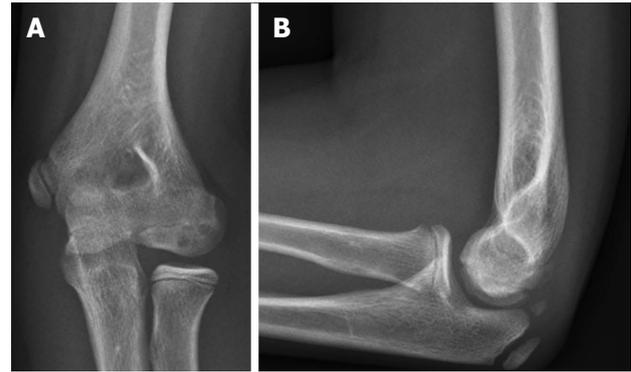


Figure 2 Plain radiography of the elbow showing an osteochondritis dissecans lesion of the capitellum. A: Anteroposterior; B: Lateral.

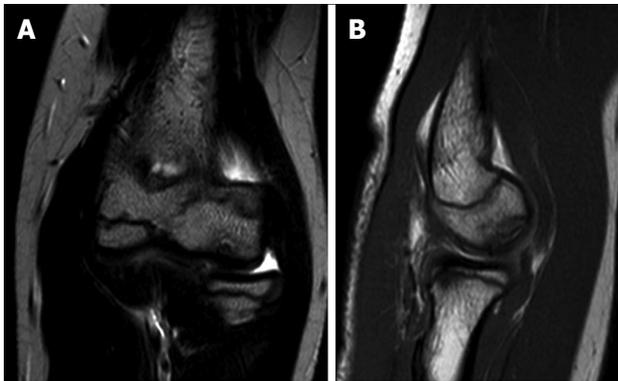


Figure 3 Magnetic resonance images of an elbow affected with osteochondritis dissecans of the capitellum. A: Coronal view; B: Sagittal view.

early OCD and is valuable in determining the stability and viability of the OCD fragment (Figure 3)^[10,17,18]. Magnetic resonance arthrography utilizes intra-articular gadolinium contrast agent to detect OCD and loose bodies^[18]. However, the addition of intra-articular contrast agent does not improve the sensitivity of MRI without contrast agent in detecting cartilage lesions in the elbow^[19]. CT scans might be more sensitive and better depict loose bodies (Figure 4). We studied 25 patients with an OCD proven by arthroscopy who all had preoperative radiographs, MRI and CT. The OCD was visible on 25 CT scans (sensitivity, 100%), on 24 MRI scans (sensitivity, 96%), and on 19 radiographs (sensitivity, 76%). Arthroscopy identified loose bodies in 20 cases. These were visible in 18 CT scans (90%), 13 MRI scans (65%) and 11 radiographs (55%). Based on these preliminary data, one might carefully conclude that CT seems to be the optimal imaging technique to diagnose OCD and loose bodies.

Classification

Although the value of grading capitellar OCD seems limited, various classifications have been described. Most are based on radiography, MRI, or arthroscopy.

Minami *et al*^[20] in 1979 described a classification

based on anteroposterior radiography. Grade 1 describes a stable lesion with a translucent cystic shadow in the capitellum; grade 2, a clear zone between the OCD and adjacent subchondral bone; and grade 3, loose bodies.

Itsubo *et al*^[21] recently introduced a T2-weighted MRI staging system that provides accurate and reliable estimation of stability of OCD. The following stages are distinguished: Stage 1, normally shaped capitellum with several spotted areas of high signal intensity that is lower than that of cartilage; stage 2, as with stage 1 but with several spotted areas of higher intensity than that of cartilage; stage 3, as with stage 2 but with both discontinuity and noncircularity of the chondral surface signal of the capitellum and no high signal interface apparent between the lesion and the floor; stage 4, lesion separated by a high intensity line in comparison with cartilage; and stage 5, capitellar lesion displaced from the floor or defect of the capitellar lesion noted. Stages 1 and 2 are considered stable. Stages 3, 4 and 5 are considered unstable^[21].

The International Cartilage Repair Society has proposed an arthroscopic classification system for OCD lesions^[22]. Grade 1 indicates a stable lesion with a continuous but softened area covered by intact cartilage; grade 2, a lesion with partial discontinuity that is stable when probed; grade 3, a lesion with a complete discontinuity that is not yet dislocated; and grade 4, an empty defect as well as a defect with a dislocated fragment or a loose fragment lying within the bed.

TREATMENT AND OUTCOMES

The treatment choice depends on several aspects, including the severity of symptoms and the size, location and stability of the lesion. It is important to differentiate between stable and unstable OCD lesions. In general, stable lesions may be reversible and can heal completely with nonoperative management, while unstable lesions need surgical treatment^[23]. Stable lesions are characterized by an immature capitellum with an open growth plate, and flattening or radiolucency of the subchondral bone, in a patient with (almost) normal elbow motion^[23,24]. Unstable lesions have at least one of

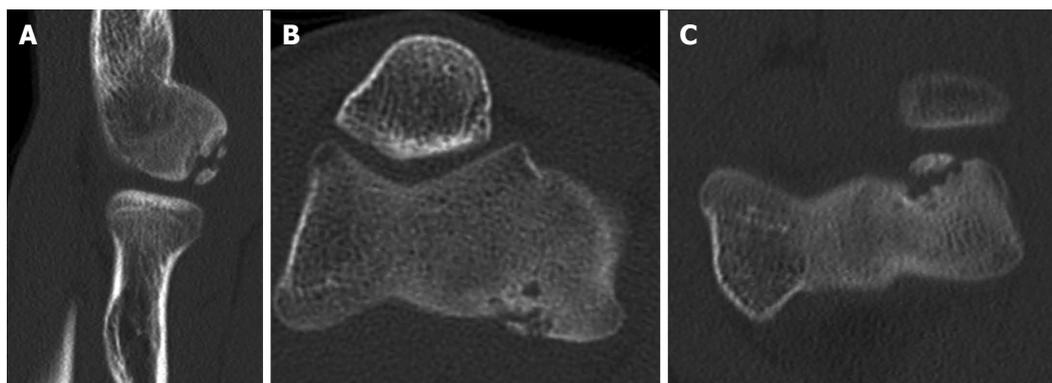


Figure 4 Computed tomography scans showing capitellar osteochondritis dissecans (A-C).

the following findings: A capitellum with a closed growth plate, fragmentation, or restriction of elbow motion 20 degrees or more^[23,25]. On MRI, unstable lesions are characterized by a high signal intensity line through the articular cartilage, a high signal intensity interface, and an articular defect^[21,26].

Nonoperative treatment

Nonoperative measures consist of rest or sports restriction (cessation of repetitive stress on the elbow), muscle strengthening exercises, non-steroidal anti-inflammatory drugs, and/or a short course of immobilization^[23,24,27]. The minority of OCD lesions are classified as stable and the initial success rates of nonoperative treatment were poor^[23,28]. Takahara *et al.*^[28] in 1999 reported a success rate of only 50% after an average follow-up of 12.6 years. Factors that are associated with the outcomes of nonoperative treatment were identified later. Bradley and Petrie reported that most patients fully recovered with complete return to sports with rest alone if they had a lesions with all of the following conditions: (1) open capitellar growth plate; (2) localized flattening or radiolucency of the subchondral bone; and (3) good elbow motion^[27]. Likewise, Mihara *et al.*^[24] showed that spontaneous healing potential of OCD in patients with open capitellar growth plates appears high. Conversely, healing potential with nonoperative management is extremely low in advanced OCD lesions with closed growth plates and in those that are unstable, even if they are undisplaced^[6,10,24,27,28].

Operative treatment

Although outcome studies on surgical treatment lack long-term follow-up and have limited methodologic quality, they generally show satisfactory results regarding pain, return to sports, and elbow function^[29]. Surgical intervention is therefore indicated for lesions that do not respond to initial nonoperative treatment and for unstable lesions^[29].

Primary surgical management most commonly consists of arthroscopic debridement of the lesion, bone marrow stimulation (by microfracturing the subchondral bone) and removal of loose fragments. Alternatively to arthroscopic surgery or for lesions after failed previous

surgery, numerous open surgical approaches have been reported, including internal fixation of large fragments and osteochondral autograft transfer^[14,30-33].

Arthroscopic treatment

Arthroscopic surgery has become the standard procedure for the treatment of capitellar OCD^[34]. It offers the advantage of direct visualization of the pathology and the ability to treat the lesion through small stab incisions. This minimally invasive approach reduces the risk of operative morbidity and allows the patient to start rehabilitation directly after surgery^[34].

Arthroscopic treatment consists of debridement of the lesion to achieve a stable rim, followed by bone marrow stimulation, and removal of any loose fragments and osteophytes^[35,36]. The patient is placed in the lateral decubitus position on the operating table. A tourniquet is placed around the upper arm, which rests on a padded arm holder that is attached to the side of the table (Figure 5). The portal sites and the ulnar nerve are marked, and the elbow is disinfected and draped. The joint is injected with 20 mL of saline solution. The complete elbow joint is inspected from anterior and posterior with use of five to six portals. A distal ulnar portal allows for ergonomic exposure to the posterolateral capitellum providing easy access for drilling, burring and local debridement^[34]. A bonecutter shaver or curette is brought into the posterolateral capitellar joint space through the standard soft-spot lateral portal. All unstable cartilage and necrotic bone are removed. Any cysts underlying the defect are opened and curetted. After debridement, several connections with the subchondral bone are created by drilling with a Kirschner wire or microfracturing with an awl (Figure 6). The objective is to partially destroy the calcified zone that is often present and to create openings into the subchondral bone. Intraosseous blood vessels are disrupted and the release of growth factors leads to the formation of a fibrin clot. The formation of local new blood vessels is stimulated, marrow cells are introduced in the defect, and fibrocartilaginous tissue is formed^[37,38].

Arthroscopic treatment has shown encouraging results at intermediate follow-up^[35,36,38,39]. Most studies report significant improvement in clinical outcome

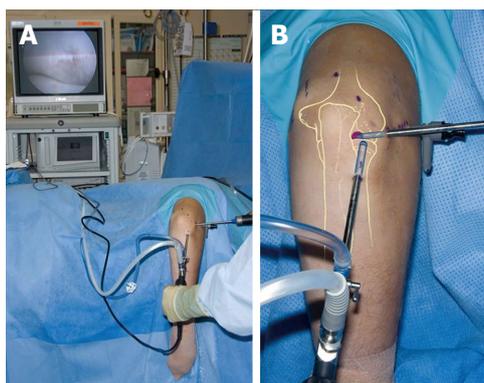


Figure 5 Patient positioning for arthroscopy of a right elbow (A and B). The patient is in the lateral decubitus position and the arm rests on a support.



Figure 6 Arthroscopic picture showing an osteochondritis dissecans lesion after debridement and microfracturing.

scores up to 9 years of follow-up^[35,36,38-40]. Approximately 80% to 90% of patients return to sports. Time to return to sports varies from 1 to 5 mo^[41-43]. Complications of elbow arthroscopy are seen in 7% to 14% of cases^[44,45]. Most complications are minor, *e.g.*, superficial wound problems and transient nerve palsies not affecting clinical outcome. Major complications occur in 0.5% to 5% of cases (*e.g.*, deep infection, permanent nerve injury, or complications requiring additional anesthesia)^[44,45].

Open surgical treatment

Refixation of the lesion can be indicated for large and (sub)acute osteochondral fragments^[31,32,46]. Different fixation techniques are available, including metal and bioresorbable screws^[31], pull-out wiring^[32,47], and cortico-cancellous bone pegs from the iliac crest or olecranon process^[3]. Cancellous bone can be additionally grafted into the defect to enhance union of the fragment^[31,32].

In follow-up studies, the clinical success rate of refixation is approximately 80%^[46-48]. Reossification is observed in 44% to 100% at follow-up^[31,32,47]. An intact lateral wall of the capitellum appears to be important for fixation to be successful^[48]. Complications have been observed in terms of intra-articular protrusion and loosening of screws^[27].

After successful application in the knee and ankle^[49], autologous osteochondral transplantation (or mosaicplasty) has been used in repairing OCD lesions of the humeral capitellum. With this technique, cylindrical osteochondral grafts are harvested from a non-weight-bearing area at the proximal aspect of the lateral femoral condyle and transplanted to the elbow to resurface the capitellar OCD.

Several authors have evaluated the technique^[30,33,50-52]. In a series of 10 patients, eight were completely pain free after a mean follow-up of 30 mo^[51]. In a recent investigation of 33 patients who were allowed to begin throwing after 3 mo and to return to sports after 6 mo, 31 patients returned to a competitive level at which they had previously played after a mean of 7 mo^[50]. Although the clinical outcomes are encouraging, the grafting technique implies damaging a healthy knee joint, possibly leading to donor-site morbidity. In a study that

addressed the effect of the harvesting on donor knee function in young athletes, a time lag was evident in recovery between postoperative symptoms and muscle power at 3 mo^[53]. However, harvesting osteochondral grafts did not exert adverse effects at 2 years after the procedure^[53].

Osteochondral autograft transfer has the advantage of replacing the affected articular surface with hyaline cartilage, but is an invasive procedure with possible donor-site morbidity. Therefore, we recommend reserving this method for revision cases after failed primary arthroscopic treatment.

Other open procedures in the literature include rib osteochondral autograft and capitellar correction osteotomy^[54-56]. Rib autografting provided satisfactory results after a follow-up of 1 to 6 years for advanced OCD with extensive lesions ≥ 15 mm and those affecting the lateral wall^[55,56]. Closed-wedge osteotomy of the capitellum has been described to widen the radiohumeral joint space, reduce compression, and stimulate revascularization and remodeling of the area of the lesion in the capitellum^[54]. Although almost all patients returned to full athletic activity, postoperative osteoarthritic changes and enlargement of the radial head occurred in all patients. Because of the few scientific data, the place of these experimental treatment methods is unclear until more evidence is available.

Postoperative rehabilitation

A physical therapist supervises the rehabilitation after surgery. Rehabilitation is aimed at reducing pain and swelling and restoring range of motion. The recovery after arthroscopic treatment is usually faster than after open surgery^[3]. Active-assisted motion exercises are started within a couple of days after surgery. After arthroscopy, the range of motion is unrestricted as pain tolerates. For patients who were treated by mosaicplasty, flexion is restricted for the first 6 wk. Resistive exercises are begun at 8 wk after arthroscopic treatment and at 12 wk after open treatment. If the patient has no pain and normal range of motion, an interval throwing program is initiated before the patient returns to sports^[3].

FUTURE DIRECTIONS

Investigations in the near future primarily should be focused on improvement of awareness and early recognition of OCD, since early intervention may prevent expansion of the lesion and future degeneration. Future studies should also aim for improvement of current treatment and development of new treatment modalities. Although outcomes of arthroscopic treatment are encouraging, larger, randomized, prospective trials are required^[29]. Likewise, promising outcomes have been described following autologous osteochondral transplantation^[50-52], but future studies should be performed with a longer follow-up time to evaluate intra-articular changes on the long term.

CONCLUSION

OCD of the elbow typically affects the humeral capitellum of adolescent throwing athletes and leads to pain on the lateral aspect of the joint. CT or MRI are indicated to confirm the diagnosis and to address stability of the lesion. Nonoperative treatment can be initiated for stable lesions. Arthroscopic surgery has become the standard primary surgical procedure for treatment of capitellar OCD. This minimally invasive approach shows good results, low risk of operative morbidity, and early recuperation postoperatively. Open surgery is indicated for more advanced cases or for those that failed previous operative treatment.

REFERENCES

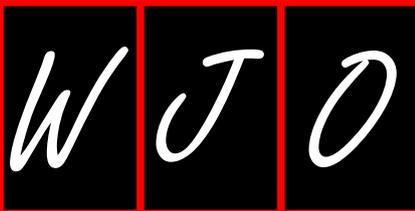
- 1 **Bruns J.** [Osteochondrosis dissecans]. *Orthopade* 1997; **26**: 573-584 [PMID: 9333747 DOI: 10.1007/PL00003414]
- 2 **Kida Y, Morihara T, Kotoura Y, Hojo T, Tachiiri H, Sukenari T, Iwata Y, Furukawa R, Oda R, Arai Y, Fujiwara H, Kubo T.** Prevalence and Clinical Characteristics of Osteochondritis Dissecans of the Humeral Capitellum Among Adolescent Baseball Players. *Am J Sports Med* 2014; **42**: 1963-1971 [PMID: 24944293 DOI: 10.1177/0363546514536843]
- 3 **Baratz M, Yi SJ.** Osteochondritis dissecans of the elbow. In: Eygendaal D, editor. The elbow. The treatment of basic elbow pathology. Nieuwegein: Arko Sports Media, 2009: 139-148
- 4 **Kenniston JA, Beredjicklian PK, Bozentka DJ.** Osteochondritis dissecans of the capitellum in fraternal twins: case report. *J Hand Surg Am* 2008; **33**: 1380-1383 [PMID: 18929205 DOI: 10.1016/j.jhssa.2008.05.008]
- 5 **Douglas G, Rang M.** The role of trauma in the pathogenesis of the osteochondroses. *Clin Orthop Relat Res* 1981; **(158)**: 28-32 [PMID: 7273524 DOI: 10.1097/00003086-198107000-00005]
- 6 **Takahara M, Ogino T, Takagi M, Tsuchida H, Orui H, Nambu T.** Natural progression of osteochondritis dissecans of the humeral capitellum: initial observations. *Radiology* 2000; **216**: 207-212 [PMID: 10887249 DOI: 10.1148/radiology.216.1.r00j129207]
- 7 **Heijink A, Gomoll AH, Madry H, Drobnič M, Filardo G, Espregueira-Mendes J, Van Dijk CN.** Biomechanical considerations in the pathogenesis of osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 423-435 [PMID: 22173730 DOI: 10.1007/s00167-011-1818-0]
- 8 **van Dijk CN, Reilingh ML, Zengerink M, van Bergen CJ.** The natural history of osteochondral lesions in the ankle. *Instr Course Lect* 2010; **59**: 375-386 [PMID: 20415393]
- 9 **van Bergen CJ, Kox LS, Maas M, Sierevelt IN, Kerkhoffs GM,**

- van Dijk CN. Arthroscopic treatment of osteochondral defects of the talus: outcomes at eight to twenty years of follow-up. *J Bone Joint Surg Am* 2013; **95**: 519-525 [PMID: 23515986 DOI: 10.2106/JBJS.L.00675]
- 10 **Bauer M, Jonsson K, Josefsson PO, Lindén B.** Osteochondritis dissecans of the elbow. A long-term follow-up study. *Clin Orthop Relat Res* 1992; **(284)**: 156-160 [PMID: 1395286]
- 11 **Takahara M, Ogino T, Sasaki I, Kato H, Minami A, Kaneda K.** Long term outcome of osteochondritis dissecans of the humeral capitellum. *Clin Orthop Relat Res* 1999; **(363)**: 108-115 [PMID: 10379311 DOI: 10.1097/00003086-199906000-00014]
- 12 **Takahara M, Shundo M, Kondo M, Suzuki K, Nambu T, Ogino T.** Early detection of osteochondritis dissecans of the capitellum in young baseball players. Report of three cases. *J Bone Joint Surg Am* 1998; **80**: 892-897 [PMID: 9655108]
- 13 **Kijowski R, De Smet AA.** Radiography of the elbow for evaluation of patients with osteochondritis dissecans of the capitellum. *Skeletal Radiol* 2005; **34**: 266-271 [PMID: 15761743 DOI: 10.1007/s00256-005-0899-6]
- 14 **Takahara M, Mura N, Sasaki J, Harada M, Ogino T.** Classification, treatment, and outcome of osteochondritis dissecans of the humeral capitellum. Surgical technique. *J Bone Joint Surg Am* 2008; **90** Suppl 2 Pt 1: 47-62 [PMID: 18310686 DOI: 10.2106/JBJS.G.01135]
- 15 **Harada M, Takahara M, Sasaki J, Mura N, Ito T, Ogino T.** Using sonography for the early detection of elbow injuries among young baseball players. *AJR Am J Roentgenol* 2006; **187**: 1436-1441 [PMID: 17114533 DOI: 10.2214/AJR.05.1086]
- 16 **Takahara M, Ogino T, Tsuchida H, Takagi M, Kashiwa H, Nambu T.** Sonographic assessment of osteochondritis dissecans of the humeral capitellum. *AJR Am J Roentgenol* 2000; **174**: 411-415 [PMID: 10658717 DOI: 10.2214/ajr.174.2.1740411]
- 17 **Takenaga T, Goto H, Nozaki M, Yoshida M, Nishiyama T, Otsuka T.** Ultrasound imaging of the humeral capitellum: a cadaveric study. *J Orthop Sci* 2014; **19**: 907-912 [PMID: 25196792 DOI: 10.1007/s00776-014-0637-9]
- 18 **Dewan AK, Chhabra AB, Khanna AJ, Anderson MW, Brunton LM.** MRI of the elbow: techniques and spectrum of disease: AAOS exhibit selection. *J Bone Joint Surg Am* 2013; **95**: e99 1-13 [PMID: 23864190 DOI: 10.2106/JBJS.L.01621]
- 19 **Theodoropoulos JS, Dwyer T, Wolin PM.** Correlation of preoperative MRI and MRA with arthroscopically proven articular cartilage lesions of the elbow. *Clin J Sport Med* 2012; **22**: 403-407 [PMID: 22929044 DOI: 10.1097/JSM.0b013e318266c735]
- 20 **Minami M, Nakashita K, Ishii S, Usui M, Muramatsu I.** Twenty-five cases of osteochondritis dissecans of the elbow. *Rinsho Seikei Geka* 1979; **14**: 805-810
- 21 **Itsubo T, Murakami N, Uemura K, Nakamura K, Hayashi M, Uchiyama S, Kato H.** Magnetic Resonance Imaging Staging to Evaluate the Stability of Capitellar Osteochondritis Dissecans Lesions. *Am J Sports Med* 2014; **42**: 1972-1977 [PMID: 24817006 DOI: 10.1177/0363546514532604]
- 22 **Brittberg M, Winalski CS.** Evaluation of cartilage injuries and repair. *J Bone Joint Surg Am* 2003; **85-A** Suppl 2: 58-69 [PMID: 12721346]
- 23 **Takahara M, Mura N, Sasaki J, Harada M, Ogino T.** Classification, treatment, and outcome of osteochondritis dissecans of the humeral capitellum. *J Bone Joint Surg Am* 2007; **89**: 1205-1214 [PMID: 17545422 DOI: 10.2106/JBJS.F.00622]
- 24 **Mihara K, Tsutsui H, Nishinaka N, Yamaguchi K.** Nonoperative treatment for osteochondritis dissecans of the capitellum. *Am J Sports Med* 2009; **37**: 298-304 [PMID: 19059891 DOI: 10.1177/0363546508324970]
- 25 **Satake H, Takahara M, Harada M, Maruyama M.** Preoperative imaging criteria for unstable osteochondritis dissecans of the capitellum. *Clin Orthop Relat Res* 2013; **471**: 1137-1143 [PMID: 22773394 DOI: 10.1007/s11999-012-2462-9]
- 26 **Kijowski R, De Smet AA.** MRI findings of osteochondritis dissecans of the capitellum with surgical correlation. *AJR Am J Roentgenol* 2005; **185**: 1453-1459 [PMID: 16303997 DOI:

- 10.2214/AJR.04.1570]
- 27 **Bradley JP**, Petrie RS. Osteochondritis dissecans of the humeral capitellum. Diagnosis and treatment. *Clin Sports Med* 2001; **20**: 565-590 [PMID: 11494842 DOI: 10.1016/S0278-5919]
 - 28 **Takahara M**, Ogino T, Fukushima S, Tsuchida H, Kaneda K. Nonoperative treatment of osteochondritis dissecans of the humeral capitellum. *Am J Sports Med* 1999; **27**: 728-732 [PMID: 10569357]
 - 29 **de Graaff F**, Krijnen MR, Poolman RW, Willems WJ. Arthroscopic surgery in athletes with osteochondritis dissecans of the elbow. *Arthroscopy* 2011; **27**: 986-993 [PMID: 21693350 DOI: 10.1016/j.arthro.2011.01.00]
 - 30 **Iwasaki N**, Kato H, Ishikawa J, Saitoh S, Minami A. Autologous osteochondral mosaicplasty for capitellar osteochondritis dissecans in teenaged patients. *Am J Sports Med* 2006; **34**: 1233-1239 [PMID: 16567456 DOI: 10.2106/jbjs.j.00214]
 - 31 **Kuwahata Y**, Inoue G. Osteochondritis dissecans of the elbow managed by Herbert screw fixation. *Orthopedics* 1998; **21**: 449-451 [PMID: 9571679]
 - 32 **Takeda H**, Watarai K, Matsushita T, Saito T, Terashima Y. A surgical treatment for unstable osteochondritis dissecans lesions of the humeral capitellum in adolescent baseball players. *Am J Sports Med* 2002; **30**: 713-717 [PMID: 12239008]
 - 33 **Vogt S**, Siebenlist S, Hensler D, Weigelt L, Ansah P, Woertler K, Imhoff AB. Osteochondral transplantation in the elbow leads to good clinical and radiologic long-term results: an 8- to 14-year follow-up examination. *Am J Sports Med* 2011; **39**: 2619-2625 [PMID: 21868690 DOI: 10.1177/0363546511420127]
 - 34 **van den Ende KI**, McIntosh AL, Adams JE, Steinmann SP. Osteochondritis dissecans of the capitellum: a review of the literature and a distal ulnar portal. *Arthroscopy* 2011; **27**: 122-128 [PMID: 21035989 DOI: 10.1016/j.arthro.2010.08.008]
 - 35 **Baumgarten TE**, Andrews JR, Satterwhite YE. The arthroscopic classification and treatment of osteochondritis dissecans of the capitellum. *Am J Sports Med* 1998; **26**: 520-523 [PMID: 9689371]
 - 36 **Byrd JW**, Jones KS. Arthroscopic surgery for isolated capitellar osteochondritis dissecans in adolescent baseball players: minimum three-year follow-up. *Am J Sports Med* 2002; **30**: 474-478 [PMID: 12130399]
 - 37 **O'Driscoll SW**. The healing and regeneration of articular cartilage. *J Bone Joint Surg Am* 1998; **80**: 1795-1812 [PMID: 9875939]
 - 38 **Wulf CA**, Stone RM, Giveans MR, Lervick GN. Magnetic resonance imaging after arthroscopic microfracture of capitellar osteochondritis dissecans. *Am J Sports Med* 2012; **40**: 2549-2556 [PMID: 23019252 DOI: 10.1177/0363546512458765]
 - 39 **Schoch B**, Wolf BR. Osteochondritis dissecans of the capitellum: minimum 1-year follow-up after arthroscopic debridement. *Arthroscopy* 2010; **26**: 1469-1473 [PMID: 20888168 DOI: 10.1016/j.arthro.2010.03.008]
 - 40 **Bojanić I**, Ivković A, Borić I. Arthroscopy and microfracture technique in the treatment of osteochondritis dissecans of the humeral capitellum: report of three adolescent gymnasts. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 491-496 [PMID: 16217674 DOI: 10.1007/s00167-005-0693-y]
 - 41 **Jones KJ**, Wiesel BB, Sankar WN, Ganley TJ. Arthroscopic management of osteochondritis dissecans of the capitellum: mid-term results in adolescent athletes. *J Pediatr Orthop* 2010; **30**: 8-13 [PMID: 20032735 DOI: 10.1097/BPO.0b013e3181c3be83]
 - 42 **Miyake J**, Masatomi T. Arthroscopic debridement of the humeral capitellum for osteochondritis dissecans: radiographic and clinical outcomes. *J Hand Surg Am* 2011; **36**: 1333-1338 [PMID: 21705155 DOI: 10.1016/j.jhsa.2011.05.024]
 - 43 **Rahusen FT**, Brinkman JM, Eygendaal D. Results of arthroscopic debridement for osteochondritis dissecans of the elbow. *Br J Sports Med* 2006; **40**: 966-969 [PMID: 16980533 DOI: 10.1136/bjsm.2006.030056]
 - 44 **Elfeddali R**, Schreuder MH, Eygendaal D. Arthroscopic elbow surgery, is it safe? *J Shoulder Elbow Surg* 2013; **22**: 647-652 [PMID: 23590887 DOI: 10.1016/j.jse.2013.01.032]
 - 45 **Nelson GN**, Wu T, Galatz LM, Yamaguchi K, Keener JD. Elbow arthroscopy: early complications and associated risk factors. *J Shoulder Elbow Surg* 2014; **23**: 273-278 [PMID: 24332953 DOI: 10.1016/j.jse.2013.09.026]
 - 46 **Henrikus WP**, Miller PE, Micheli LJ, Waters PM, Bae DS. Internal Fixation of Unstable In Situ Osteochondritis Dissecans Lesions of the Capitellum. *J Pediatr Orthop* 2014; **35**: 467-473 [PMID: 25264554 DOI: 10.1097/BPO.0000000000000308]
 - 47 **Nobuta S**, Ogawa K, Sato K, Nakagawa T, Hatori M, Itoi E. Clinical outcome of fragment fixation for osteochondritis dissecans of the elbow. *Ups J Med Sci* 2008; **113**: 201-208 [PMID: 18509814 DOI: 10.3109/2000-1967-232]
 - 48 **Kosaka M**, Nakase J, Takahashi R, Toratani T, Ohashi Y, Kitaoka K, Tsuchiya H. Outcomes and failure factors in surgical treatment for osteochondritis dissecans of the capitellum. *J Pediatr Orthop* 2013; **33**: 719-724 [PMID: 23774205 DOI: 10.1097/BPO.0b013e3182924662]
 - 49 **Hangody L**, Füles P. Autologous osteochondral mosaicplasty for the treatment of full-thickness defects of weight-bearing joints: ten years of experimental and clinical experience. *J Bone Joint Surg Am* 2003; **85-A** Suppl 2: 25-32 [PMID: 12721342]
 - 50 **Maruyama M**, Takahara M, Harada M, Satake H, Takagi M. Outcomes of an open autologous osteochondral plug graft for capitellar osteochondritis dissecans: time to return to sports. *Am J Sports Med* 2014; **42**: 2122-2127 [PMID: 24950681 DOI: 10.1177/0363546514538759]
 - 51 **Ovesen J**, Olsen BS, Johannsen HV. The clinical outcomes of mosaicplasty in the treatment of osteochondritis dissecans of the distal humeral capitellum of young athletes. *J Shoulder Elbow Surg* 2011; **20**: 813-818 [PMID: 21208812 DOI: 10.1016/j.jse.2010.09.001]
 - 52 **Lyons ML**, Werner BC, Gluck JS, Freilich AM, Dacus AR, Diduch DR, Chhabra AB. Osteochondral autograft plug transfer for treatment of osteochondritis dissecans of the capitellum in adolescent athletes. *J Shoulder Elbow Surg* 2015; **24**: 1098-1105 [PMID: 25958215 DOI: 10.1016/j.jse.2015.03.014]
 - 53 **Nishimura A**, Morita A, Fukuda A, Kato K, Sudo A. Functional recovery of the donor knee after autologous osteochondral transplantation for capitellar osteochondritis dissecans. *Am J Sports Med* 2011; **39**: 838-842 [PMID: 21189356 DOI: 10.1177/0363546510388386]
 - 54 **Kiyoshige Y**, Takagi M, Yuasa K, Hamasaki M. Closed-Wedge osteotomy for osteochondritis dissecans of the capitellum. A 7- to 12-year follow-up. *Am J Sports Med* 2000; **28**: 534-537 [PMID: 10921645]
 - 55 **Nishinaka N**, Tsutsui H, Yamaguchi K, Uehara T, Nagai S, Atsumi T. Costal osteochondral autograft for reconstruction of advanced-stage osteochondritis dissecans of the capitellum. *J Shoulder Elbow Surg* 2014; **23**: 1888-1897 [PMID: 25240513 DOI: 10.1016/j.jse.2014.06.047]
 - 56 **Shimada K**, Tanaka H, Matsumoto T, Miyake J, Higuchi H, Gamo K, Fuji T. Cylindrical costal osteochondral autograft for reconstruction of large defects of the capitellum due to osteochondritis dissecans. *J Bone Joint Surg Am* 2012; **94**: 992-1002 [PMID: 22637205 DOI: 10.2106/JBJS.J.00228]

P- Reviewer: Schmitz MR S- Editor: Ji FF
L- Editor: A E- Editor: Liu SQ





Tumors of the spine

Mert Ciftdemir, Murat Kaya, Esref Selcuk, Erol Yalniz

Mert Ciftdemir, Murat Kaya, Esref Selcuk, Erol Yalniz, Department of Orthopaedics and Traumatology, Trakya University School of Medicine, 22030 Edime, Turkey

Author contributions: Ciftdemir M wrote the manuscript, helped in literature review and making the tables, and checked the references; Kaya M, Selcuk E and Yalniz E performed the literature review and drafted the article; all authors approved the final version of the manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest related to the work.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Mert Ciftdemir, MD, Assistant Professor, Department of Orthopaedics and Traumatology, Trakya University School of Medicine, Balkan Yerleskesi, 22030 Edime, Turkey. dr.mert@gmail.com
Telephone: +90-532-7653385
Fax: +90-284-2133899

Received: May 12, 2015

Peer-review started: May 18, 2015

First decision: August 19, 2015

Revised: September 20, 2015

Accepted: November 13, 2015

Article in press: November 17, 2015

Published online: February 18, 2016

Abstract

Spine tumors comprise a small percentage of reasons for back pain and other symptoms originating in the spine. The majority of the tumors involving the spinal column are metastases of visceral organ cancers which are mostly seen in older patients. Primary musculoskeletal

system sarcomas involving the spinal column are rare. Benign tumors and tumor-like lesions of the musculo-skeletal system are mostly seen in young patients and often cause instability and canal compromise. Optimal diagnosis and treatment of spine tumors require a multidisciplinary approach and thorough knowledge of both spine surgery and musculoskeletal tumor surgery. Either primary or metastatic tumors involving the spine are demanding problems in terms of diagnosis and treatment. Spinal instability and neurological compromise are the main and critical problems in patients with tumors of the spinal column. In the past, only a few treatment options aiming short-term control were available for treatment of primary and metastatic spine tumors. Spine surgeons adapted their approach for spine tumors according to orthopaedic oncologic principles in the last 20 years. Advances in imaging, surgical techniques and implant technology resulted in better diagnosis and surgical treatment options, especially for primary tumors. Also, modern chemotherapy drugs and regimens with new radiotherapy and radiosurgery options caused moderate to long-term local and systemic control for even primary sarcomas involving the spinal column.

Key words: Spinal column; Sarcoma; Metastasis; Spinal neoplasms; Palliative surgery

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Primary tumors involving the spine are rare, while spinal column metastases are present in up to 70% of cancer patients. Both primary and metastatic tumors of the spine are often asymptomatic or have non-specific symptoms because in spine tumors, delayed diagnosis is not very unusual. Goal of treatment in spinal column metastases is to optimize the patient's quality of life by providing effective pain relief and preserving or restoring neurological functions. Treatment strategy for primary tumors should be planned after both oncological and surgical staging. Because of that, biopsy is a very important step in primary tumors. Surgery in metastatic

tumors are mostly palliative, aiming short-term control. Primary benign and malignant lesions mainly cause canal compromise and are treated surgically according to oncological staging and Weinstein-Boriani-Biagini classification.

Ciftdemir M, Kaya M, Selcuk E, Yalniz E. Tumors of the spine. *World J Orthop* 2016; 7(2): 109-116 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/109.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.109>

INTRODUCTION

Spine tumors are examined under two subtitles called primary tumors which originate from the spine itself and its adjacent structures and secondary (metastatic) tumors of distant organs which spread hematogenously and lymphatically and are located in the spine and its surrounding tissues. As the spine is well vascularized and has close relationship with regional lymphatic and venous drainage systems (especially Batson's venous plexus), it is generally susceptible to metastasis. Metastatic tumors are most common (97%) tumors of the spine^[1]. It is known that the adenocarcinomas which mostly originate from the lung, breast, prostate, kidney, gastrointestinal tract and thyroid tend to metastasize especially to the spine^[2]. It was found that the percentage of cancer patients who have had bone metastasis before death is between 50% and 70%, and especially in case of breast cancer this percentage rose up to 85%. Up to 10% of patients who have symptomatic spine metastases can be treated by surgery^[3]. The most common (70%) sites for spine metastasis are thoracic and thoracolumbar spine, and lumbar spine and sacrum have more than 20% of metastatic lesions. Cervical spine is a less frequent metastasis site^[1].

As primary tumors of the spine are rare and most of these lesions are asymptomatic, their real incidence is unknown. It is estimated that the incidence of hemangiomas and enostoses, which were accepted as the most common primary tumors of the spine, is between 11% and 14%. This ratio has been found to be dependent on lesions which have been detected incidentally in performing diagnostic procedures for another reasons. Proper diagnosis of these asymptomatic lesions which are seen in the spine very common and do not require treatment will prevent the performance of unnecessary diagnostic procedures^[3]. Except some primary tumors (osteoblastoma, chordoma) which tend to effect especially the spine, tumors originate from the skeleton system itself are not seen in the spine frequently. Differential diagnosis of primary tumors of the spine from especially spinal infections is extremely important. Primary malignant tumors of the spine is the rarest tumor type in the spine. In all bone and soft tissue sarcomas, only 10% of them are related with the spine^[4].

Clinical features

Patients with spine tumors have medical histories and physical examination findings which are not directly associated with current disease. However, these findings need to be perfectly understood and evaluated in order to give some clues about the disease to the physician. In patients with spine tumors, the most common and leading symptom is pain^[4]. As in almost all skeletal system tumors, the patients with spine tumors believe that their pain is relevant to a real or suspected traumatic event in the recent past. This condition sometimes indicates a pathological fracture which occurs by collapsing of the vertebral body due to a current destruction as a result of a minor trauma. The pain that slowly starts, gradually increases, is usually persistent at night and eventually disturbs the patient even at rest is considered the most typical sign for spine tumors. An acute pain that starts without any trauma in a patient without any previous symptom should also be considered a pathological fracture. Pain in spinal tumors can occur as a result of many reasons. Generally a tumor that grows inside the vertebral body with expansion causes bone remodeling and thinning of the cortex at first, then causes pathologic fracture and invasion of paravertebral structures. At the beginning of disease the main source of pain is stretched periosteum as a result of cortical expansion. After the development of the fracture, pain due to neural compression, neurological deficits and instability comes foreground^[3]. Waist and back pain is commonly seen in the population. However, most patients with spine tumors have local tenderness which is a sign that was not observed in other non-traumatic spine problems. Benign tumors in children can sometimes appear as secondary scoliosis or torticollis due to pain. In the case of pathological fracture, kyphotic posture may be seen.

In patients with spine tumors, radicular signs are also frequent. Radicular signs could also be as a result of invasion or compression of the nerve root by the tumor itself, and sometimes pathologic fractures could make root irritation. In patients who developed a neurological deficit, it is important to evaluate the processes associated with the development of this deficit^[4]. There is a major difference in terms of prognosis and behavior of the tumor between a patient with a sudden onset of paraparesia and paraplegia who previously had pain and a patient who developed a neurological deficit in months.

Another important point about evaluating patients with spine tumors is the patient's age. Metastatic tumors, which are the most common tumors of the spine, and hematological malignancies are usually seen after 50 years of age.

In cases under the age of 18, usually benign primary bone tumors such as hemangiomas, eosinophilic granuloma, osteoid osteoma, osteoblastoma, aneurysmal bone cyst and giant cell tumor should be considered in the foreground^[3,5]. The most common malignant

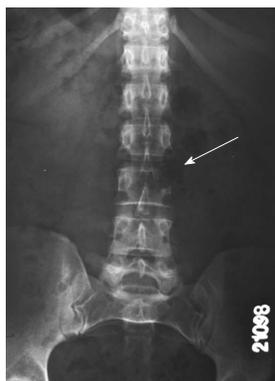


Figure 1 The (absent) pedicle sign known as the winking owl sign (arrow). A reliable sign of osteolytic spinal metastases on antero-posterior radiographs is loss of the normal pedicle contour.

tumors in young patients are osteosarcoma and Ewing's sarcoma^[3].

When evaluating patients with spine tumors, the current and potential cancer and carcinogen contact history must be investigated. There are reports about cases who had spine metastases years after successful cancer treatment^[3]. It must be kept in mind that benign musculoskeletal lesions in any part of the body may cause spine metastasis after malignant or sarcomatous transformation^[6]. Especially history of mammographic examination in female patients over 40 years of age, and the smoking history in male patients must be questioned^[4].

Diagnostic procedures

Plain radiographs must always take the first line in imaging for spinal diseases. In patients with suspected spine tumors, other parts of the spine and pelvis must be screened in addition to the plain radiographs of the suspected region. Plain radiographs can help to identify nearly 80% of the benign tumors that have a more specific appearance and some of malignant tumors and metastatic lesions^[1]. Plain radiographic findings are present in 40% of patients with spine metastasis. At least 50% loss of the trabecular bone is required for a destructive spine lesion to be visualised on plain radiographs^[4]. In many hematological malignancies, plain radiographic findings may not be seen until the advanced stages of disease. Plain radiographic characteristics of metastatic lesions can be osteoblastic, osteolytic or mixed. Spine metastases of prostate and breast carcinomas are generally osteoblastic or mixed-type lesions, but lung and thyroid carcinomas as well as renal cell carcinoma are usually in the form of lytic metastatic lesions^[3].

Radiopaque lesions which extend outside of the rectangle that draws the boundaries of the vertebral body generally indicate primary malignant lesions of the spine like osteosarcoma or chondrosarcoma. Radiographic sign known as "winking owl sign" can be defined as a faint shadow obscuring the visibility of one pedicle on anteroposterior radiograph, indicates extending of the

tumor mass from vertebral body to paraspinal area (Figure 1). Winking owl sign is generally accepted as the earliest direct radiographic sign of a metastatic lesion. Another plain radiographic finding for spine tumors is presence of one or more lytic lesions. Lytic lesions indicate bone destruction. However, destruction pattern gives information about nature of the tumor in the spine as well as in all bone tumors. Geographical destruction suggests that tumor is slowly progressive, moth-eaten lesions suggest that tumor grows faster, and permeative destruction suggests that tumor is very rapidly progressive^[5]. Another plain radiographic finding is collapse of the vertebral body that can be called compression fracture. It is not easy to distinguish pathological compression fractures from benign osteoporotic ones. Bone scintigraphy is the most helpful diagnostic procedure in cases whose plain radiographs are negative or suspicious^[4]. Bone scintigraphy is a diagnostic procedure performed by radioisotopes. Even though bone scintigraphy has a low specificity except in some tumors such as osteoid osteoma, it is a useful tool for diagnosis because of its high sensitivity and the ability to scan the entire body that is not found in other diagnostic tools. It is also useful in terms of recognizing the primary disease in metastatic tumors which have unknown primary origins and guiding biopsy.

Computed tomography (CT) is the most advantageous method in examination of mineralized tissues. Even complex anatomical structures like the spine could be evaluated by CT, which is superior to plain radiographs with regards to its ability of 3 plane examination. However, poor affinity and efficacy of CT in soft tissue lesions are disadvantages of this method.

Magnetic resonance imaging (MRI) is superior to all diagnostic procedures in spine tumors, especially in the evaluation of bone marrow and spinal canal, relationship of the tumor with neurovascular structures and tumor vascularity. In patients with spinal canal involvement, MRI is a useful technique for scanning the adjacent levels with wide, cross-sectional sagittal images. In 10% of spine metastases with spinal canal involvement, neurological compromise in adjacent or distant levels has been shown^[3]. An important point about the MRI is its ability to differentiate osteoporotic compression fractures and pathological spinal fractures. Although there is no consensus so far, pathological fractures show low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences, but osteoporotic compressions show low signal intensity in both sequences. However, this finding is not valid for acute osteoporotic fractures. Osteoporotic compression fractures in the acute state (3-6 wk after the fracture) will be able to show low signal intensity on T1-weighted sequences and high signal intensity on T2-weighted sequences due to oedema and congestion within the trabecular bone. In such cases, the bone marrow signal pattern should be evaluated. Gadolinium contrast enhanced MRI can also distinguish intra and extra-dural tumors and also intra and extra-medullary tumors^[7].

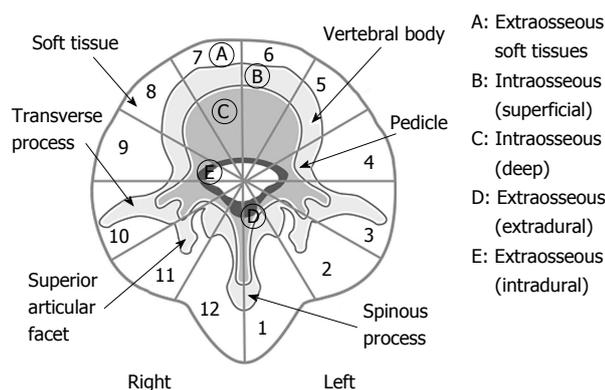


Figure 2 The Weinstein-Boriani-Biagini surgical staging system^[13]. In this classification, the spine is radially divided into 12 equal radial segments (clock-face) in axial plane and examined in 5 layers from superficial to deep plane. Adapted with permission from Spine 1997; 22(9):1036-1044.

In spine tumors, especially those with unknown primary origin, biopsy is the latest and the most crucial step of the diagnostic process. Before planning the biopsy, all diagnostic tools should be used in a rational manner and precise localization of the lesion should be determined^[8]. Biopsy in spine tumors can be performed as fine needle aspiration, tru-cut biopsy, incisional or excisional biopsy. Fine needle biopsy and tru-cut biopsy are percutaneously applied procedures. It should be kept in mind that biopsy tract is contaminated by tumor cells, and biopsies must be performed far from the neurovascular structures by small incisions which could then be removed with tumor mass in definitive surgical procedure.

Staging

In orthopedic oncologic surgery, where multidisciplinary approach is necessary, use of classifications that guide the treatment steps is inevitable^[9]. The effective use of these classifications requires knowledge about the surgical margins in orthopedic oncologic surgery. Surgical treatment of bone tumors should be performed by targeting one of the four surgical margins^[10]. In intralesional surgery, the tumor is removed in small pieces by destroying the anatomical structure and integrity of tumor. This type of surgery is usually performed in benign tumors, because it is not possible to obtain a clean surgical margin by this method. In marginal resection, the tumor is removed *en bloc* but, even in a small area of its surface, it is covered by the capsule or pseudocapsule. In wide resection, the tumor is removed *en bloc* entirely enwrapped by a continuous layer of normal tissue. Finally, in the radical resection, the tumor is removed *en bloc* with the entire anatomical compartments of origin bounded by its natural barriers such as the disc, fascia, cortex and end plate^[11].

Enneking classification has been used for the classification of benign and malignant tumors of the musculoskeletal system for over 25 years^[12]. In Enneking classification, benign tumors are indicated with arabic numbers (1, 2, 3) according to the nature of tumor and

its histopathological grade. Benign tumors are classified as inactive (latent), active and aggressive. Malignant tumors are indicated with Roman numbers (I, II, III) according to histopathological grade, localization and the relationship of tumor with natural barriers and whether the tumor metastasizes or not^[12]. However, Enneking classification in treatment of spine tumors has been found to be insufficient for surgical planning over time. Because of that, in 1997, Boriani *et al.*^[13] have published a study about the new terminology and surgical staging for primary tumors of the spine. The authors stated a new classification system known as Weinstein-Boriani-Biagini classification, which is still actively in use today. In this classification, the spine is radially divided into 12 equal radial segments (clock-face) in axial plane and examined in 5 layers from superficial to deep plane (Figure 2).

In 2005, Tokuhashi *et al.*^[14] have published a study about preoperative prognostic classification for patients with spine metastases. The classification system was based on general condition of the patient, extraspinal bone metastases, number of metastatic foci in the spine, major visceral metastases, primary cancer focus (origin) and the patient's neurological status. The authors have stated that the patients with a Tokuhashi score between 12 and 15 points have a life expectancy more than 1 year and this patient group should be treated by tumor excision. The patients with a Tokuhashi score between 9 and 11 points have a life expectancy more than 6 mo, and patients in this group with single level spine metastasis but without major internal organ (visceral) metastases should be treated by tumor excision, while the rest should be treated by palliative surgery. The patients with a Tokuhashi score less than 8 points have a life expectancy less than 6 mo, and these patients should be treated by palliative surgery or conservative treatment^[14].

Tomita *et al.*^[15] have published a classification regarding surgical strategy in spinal metastases in 2001. According to this classification, patient evaluation was based on 3 prognostic factors: Histopathologic grade of primary tumor, visceral metastasis to vital organs (the lungs, liver, kidneys and brain) and bone metastases including spine metastases (Table 1). Spine metastases were also evaluated in 7 types (Figure 3). As long-term regional control could be provided, the patients whose score is 2-3 points from Tomita classification are suggested to be treated by total *en bloc* spondylectomy which means marginal or wide resection; as medium-term regional control could be provided, the patients whose score is 4-5 points are suggested to be treated by marginal resection or intralesional treatment (total *en bloc* spondylectomy or curettage); as they are appropriate for short-term palliation, the patients whose score is 6-7 points are suggested to be treated by palliative surgery like spinal canal decompression and stabilization; the patients whose score is 8 and above points are suggested to be treated by conservative support treatment instead of surgical treatment with the

Table 1 Surgical strategy for spinal metastases

Point	Scoring system			Prognostic score	Treatment goal	Surgical strategy
	Prognostic factors					
	Primary tumor	Visceral metastases	Bone metastases ¹			
1	Slow growth (breast, thyroid, <i>etc.</i>)		Solitary or isolated	2	Long-term local control	Wide or marginal excision
2	Moderate growth (kidney, uterus, <i>etc.</i>)	Treatable	Multiple	3		
4	Rapid growth (lung, stomach, <i>etc.</i>)	Untreatable		4	Middle-term local control	Marginal or intralesional excision
				5		
				6	Short-term palliation	Palliative surgery
				7		
				8	Terminal care	Supportive care
				9		
				10		

No visceral metastases = 0 points; ¹Bone metastases: Including spinal metastases.

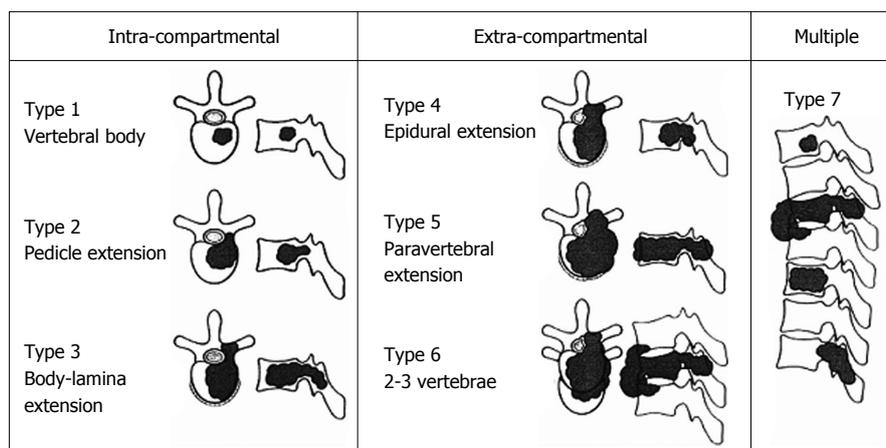


Figure 3 Schematic diagram of surgical classification of spinal tumors according to Tomita *et al.*^[15]. Adapted with permission from Spine 2001; 26(3): 298-306.

idea that they are at the terminal stage.

Surgical treatment

In spine tumors, main goal of surgical treatment is local control for local disease and at least one year survival for spine metastases. Surgery is the best treatment option for the pain and neurological symptoms caused by spinal instability. Spinal instability, vertebral collapse with or without any neurological deficit, radiotherapy resistant tumors, intolerable pain unresponsive to conventional therapy and neurological deficit before, during or after the radiotherapy are the indications for surgery^[7]. General principals for spine tumor surgery are decompression of tumor compression to the spinal cord, establishing a tumor-free solid spine and performing the surgery with minimal morbidity.

Surgical modalities in metastatic spine tumors are palliative interventions including posterior decompression of spinal canal with posterior instrumentation, restoring the bone loss of the vertebral body with cement augmentation techniques (vertebroplasty/kyphoplasty), and total spondylectomy with anterior and posterior stabilization^[15]. In primary tumors of the spine, total/partial laminectomy, total/partial vertebral body resection, piece-meal resection and curettage, in addition to the surgical procedures described above, can be used.

Total spondylectomy or vertebrectomy, which is the wide resection procedure for spine tumors, can be performed in 1 or 2 stage operation. In 2 stage total spondylectomy, initially posterior instrumentation is applied and total laminectomy *via* bilateral pedicle section is done. After that, the patient is turned in supine position and vertebral body removal is performed *via* an anterior approach. In total spondylectomy, segmentary nerve roots and vessels are ligated and sectioned as well as caudal and cranial discs. After vertebral body removal, anterior defect must be reconstructed^[13]. One stage total *en bloc* spondylectomy was introduced by Tomita *et al.*^[16]. In this procedure, removal of vertebral body is performed through a posterior approach after blunt dissection of vertebral body from surrounding structures and large vessels that lie at the anterior of the spinal column^[16] (Table 2).

Radical resection is not easy in spine tumors. According to surgical oncologic principles, total removal of involved level vertebral body as well as that level of dural sac, spinal cord and spinal nerves have to be sectioned^[13]. Even though this procedure is extremely morbid, it is rarely used as a salvage procedure^[7].

Primary benign spinal tumors

Osteoid osteoma, osteoblastoma, osteochondroma,

Table 2 Tokuhashi classification^[14]

Characteristic	Score
General condition (performance status)	
Poor (10%-40%)	0
Moderate (50%-70%)	1
Good (80%-100%)	2
No. of extraspinal bone metastasis foci	
≥ 3	0
1-2	1
0	2
No. of extraspinal metastasis foci in the vertebral body	
≥ 3	0
1-2	1
0	2
Metastases to the major internal organs	
Unremovable	0
Removable	1
No metastases	2
Primary site of the cancer	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gallbladder, unidentified	1
Others	2
Kidney, uterus	3
Rectum	4
Thyroid, breast, prostate, carcinoid tumor	5
Palsy	
Complete (Frankel A, B)	0
Incomplete (Frankel C, D)	1
None (Frankel E)	2

Criteria of predicted prognosis: Total score (TS) 0-8: < 6 mo; TS 9-11: ≥ 6 mo; TS 12-15: ≥ 1 year.

giant cell tumor of the bone, aneurysmal bone cyst, eosinophilic granuloma and neurofibroma are the most common primary benign spine tumors. Primary benign tumors of the spine are more common than primary malignant ones. Benign aggressive tumors, such as giant cell tumor of the bone, osteoblastoma and aneurysmal bone cyst, tend to relapse. Because of that, surgical treatment of these tumors must include local adjuvant agents with marginal resection^[17].

Osteochondromas as they are mostly seen in the other benign tumors of the spine, originate from posterior elements and become symptomatic by spinal canal compromise or nerve root compression. One should not forget that, if the cartilage cap of the osteochondroma is not completely removed, the tumor can recur^[18].

Osteoid osteoma is a frequent primary benign spinal tumor. Osteoid osteoma is commonly seen in adolescents and young adults with painful secondary scoliosis and pain that worsens at night and is relieved by non-steroidal anti-inflammatory agents, especially acetyl-salicylate. Treatment of osteoid osteoma is based on removal or ablation of entire nidus. Symptoms dramatically disappear after treatment^[19].

The most common site for osteoblastoma in the entire skeleton is the spinal column. Although histopathologically similar to osteoid osteoma, osteoblastoma has different clinical and radiological characteristics. Osteoblastomas mostly originate from posterior elements, as other benign tumors. In contrast to osteoid osteoma, osteoblastoma

can grow into the spinal canal and may cause dural sac compression. Treatment of osteoblastomas consists of intralesional excision or marginal resection according to histopathological grade. Postoperative radiotherapy may be feasible in terms of local control in some cases^[20].

Hemangioma is the most frequent benign tumor involving the spinal column. Typically hemangiomas involve vertebral body and they are usually asymptomatic lesions. According to autopsy findings, hemangiomas are seen in 10% of the general population^[3]. Even though hemangiomas are asymptomatic, they may cause pathological fractures. Also, hemangiomas can cause symptoms in the 3rd trimester of pregnancy.

Aneurysmal bone cysts (ABC) are commonly seen in the posterior elements of the spinal column in patients under the age of 20. ABC have a tendency to involve more than one segment. ABC are continuously growing and expanding active or aggressive (stage 2-3) lesions. Treatment of ABC consists of embolization or wide resection after embolization. ABC have an overall recurrence rate of 25%^[21].

Giant cell bone tumor (GCT) is commonly seen in the sacrum more than other parts of the spinal column. It is difficult to obtain clean surgical margins in the surgical treatment of GCTs because of their localization within the vertebral body. Surgical margins should aim wide resection, because piece-meal removal is associated with a recurrence rate of 50% in surgical treatment of GCT. Postoperative radiotherapy for local control is controversial because of high risk of sarcomatous transformation. This transformation is generally to secondary osteosarcoma. Even though GCT is a benign tumor, it is capable of lung metastasis.

Eosinophilic granuloma is a benign tumor which is more often seen in children and adolescents. Eosinophilic granuloma generally causes uniform, rapid flattening of the vertebral body. Radiological appearance of this type of vertebral body involvement is called vertebra plana^[3]. Always it heals spontaneously. Classical treatment is observation and bracing in some cases to prevent development of kyphosis.

Primary musculoskeletal system sarcomas in spine

Three types of major primary musculoskeletal system sarcomas that are mostly seen in the spinal column are osteosarcoma, Ewing's sarcoma and chondrosarcoma. These tumors can be seen in any part of the entire spinal column. Osteosarcoma and Ewing's sarcoma are more often seen in children and adolescents but chondrosarcomas are more often seen in adults and older individuals^[22].

Ewing's sarcoma is more frequent in patients between the age of 5 and 20. Because of the inflammatory characteristics of Ewing's sarcoma, this tumor may be misdiagnosed as infection and diagnosis can be delayed^[1]. Swelling, local tenderness, fever and increase in sedimentation rate are the significant characteristics of patients with Ewing's sarcoma. Spinal column involvement is seen in only 5% of patients with Ewing's

sarcoma. In patients with axial skeleton involvement, Ewing's sarcoma is most commonly seen in the pelvis. In contrast to long bones in which periosteal reaction and permeative destruction are predominant, lytic lesions associated with soft tissue masses in the vertebral body is the main radiological finding of spine involvement of Ewing's sarcoma. Preservation of contiguous discs help to distinguish Ewing's sarcoma from spondylodiscitis. In pediatric spinal infections, disease generally starts from disc space and extends to vertebral end plates, but in Ewing's sarcoma involvement starts from the core trabecular bone of the vertebral body, and endplate involvement may be seen in late phase of the tumor invasion^[7]. Because of high cellularity of the tumor tissue, Ewing's sarcomas located in extremities and the spine respond well to chemotherapy. Wide resection with clear surgical margins is possible after neo-adjuvant chemotherapy in Ewing's sarcoma. Postoperative radiotherapy should be given in cases with contaminated surgical margins^[5].

Even though osteosarcoma is the most commonly seen primary malignant tumor of bone, spinal involvement is rare. Approximately 2% of all osteosarcomas originate from the spine. Classic osteosarcoma is most commonly seen in the second decade of life. Occasionally, osteosarcoma may have its second peak incidence in the 6th decade of life as secondary osteosarcomas which arise from sarcomatous transformation of presarcomatous lesions such as Paget's disease of bone and fibrous dysplasia^[3]. Paget's osteosarcomas more commonly occur in the spine and pelvis. Treatment of osteosarcomas involving the spinal column is similar to that for extremity osteosarcomas. Treatment of osteosarcoma has evolved in the last 40 years. Before 1970s, 5-year-survival rate was 10% for osteosarcomas, with 70%-80% of the patients surviving with no evidence of disease today. Current treatment of osteosarcoma consists of 2 episodes of neoadjuvant chemotherapy followed by wide or radical resection and at least 4 more chemotherapy episodes. Tumor response to chemotherapy is important for prognosis^[3,5].

Chondrosarcomas are more common than the other primary sarcomas in the spine. As a result of highly avascular characteristics of cartilage tissue, chondrosarcoma is unresponsive to chemotherapy and radiotherapy so that main determinative for prognosis is surgical treatment with wide or radical surgical margins^[3]. In surgical treatment main target should address radical resection.

Chordoma does not originate from the musculoskeletal system, and this tumor arises from remnants of the notochordal cells. Even though it is not a primary skeletal tumor, chordoma involves the spinal column and affects mainly the sacrum and lower lumbar vertebrae with its destructive behaviour. Chordoma is one of the most common tumors of the sacrum. While 60% of chordomas arise in the sacrum, 25% are seen at the skull base and the remaining 15% seen in the rest of the axial skeleton^[23]. Chordomas are generally

seen in the midline and caudal half of the sacrum (S3 and more caudal levels). Constipation, coccygodynia, hemorrhoids and urinary incontinence are the most common symptoms. Half of the sacral chordomas are palpable in digital rectal examination. As an original soft tissue tumor, chordoma is best evaluated using MRI. Surgical margins have great importance in prognosis of chordoma, therefore especially in the treatment of sacral chordoma wide resection should be aimed.

CONCLUSION

Spinal column represents the major portion of the axial skeleton that supports vital organs. Metastatic tumors are the most frequent tumors that involve the spine. In terms of frequency, benign bone tumors follow the metastatic tumors and primary bone sarcomas are the least frequent tumors that involve the spine. Sometimes it is difficult to distinguish primary tumors from metastatic tumors in the spine. Metastatic tumors with unknown origin are also common in the spine. Knowledge about the primary lesion has critical importance in treatment protocol for metastatic tumors of the spine. Therefore, in primary unknown metastases, biopsy is an important step which affects the treatment modalities. It should be kept in mind that metastatic lesions that involve the spinal are a part of systemic malignancies. Surgical staging is important for determining treatment protocol. Treatment of metastatic tumors should aim pain relief with preservation of mechanical and neurological functions of the spine. In primary tumors treatment strategy should address removal of local disease while preserving the mechanical and neurological functions of the spine. As in all oncological surgery procedures, all diagnostic and interventional procedures in primary or metastatic tumors of the spine, as well as the general management of the patient should be performed in a multidisciplinary approach.

REFERENCES

- 1 **Lewandrowski KU**, Anderson ME, McLain RF. Tumors of the Spine. In: Herkowitz HN, Garfin SR, Eismont FJ, Bell GR, Balderston RA. Philadelphia: Elsevier Saunders, 2011: 1480-1512 [DOI: 10.1016/B978-1-4160-6726-9.00085-7]
- 2 **Choi D**, Crockard A, Bungler C, Harms J, Kawahara N, Mazel C, Melcher R, Tomita K. Review of metastatic spine tumour classification and indications for surgery: the consensus statement of the Global Spine Tumour Study Group. *Eur Spine J* 2010; **19**: 215-222 [PMID: 20039084]
- 3 **Aboulafia AJ**, Levine AM. Musculoskeletal and Metastatic Tumors. In: Fardon DF, Garfin SR. OKU: Spine 2, Rosemont. American Academy of Orthopaedic Surgeons, 2002: 411-431
- 4 **Deol GS**, Haydol R, Phillips FM. Tumors of the Spine. In: Vaccaro AR. OKU 8, Rosemont. American Academy of Orthopaedic Surgeons, 2005: 587-599
- 5 **Boos N**, Fuchs B. Primary Tumors of the Spine. In: Boos N, Aebi M. Spinal disorders: Fundamentals of Diagnosis and Treatment. Berlin: Springer-Verlag, 2008: 951-976 [DOI: 10.1007/978-3-540-69091-7]
- 6 **Boriani S**, Bandiera S, Casadei R, Boriani L, Donthineni R, Gasbarrini A, Pignotti E, Biagini R, Schwab JH. Giant cell tumor of the mobile spine: a review of 49 cases. *Spine (Phila Pa 1976)*

- 2012; **37**: E37-E45 [PMID: 22179322 DOI: 10.1097/BRS.0b013e3182233ccd]
- 7 **Davies AM**, Cassar-Pullicino VN. Principles of Detection and Diagnosis. In: Davies AM, Sundaram M, James SLJ. Imaging of Bone tumors and Tumor-like Lesions. Berlin: Springer-Verlag, 2009: 111-135 [DOI: 10.1007/978-3-540-77984-1_7]
 - 8 **Aebi M**. Spinal Metastasis in the Elderly. In: Aebi M, Gunzburg R, Szpalski M. Aging Spine. Berlin: Springer-Verlag, 2005: 120-131 [DOI: 10.1007/s00586-003-0609-9]
 - 9 **Copuroglu C**, Yalniz E. Spinal oncologic reconstruction. *World Spinal Column J* 2010; **1**: 176-183
 - 10 **Campanacci M**. Bone and Soft Tissue Tumors. 2nd ed. Padova: Piccin Nuova Libraria, 1999: 46-52 [DOI: 10.1007/978-3-7091-3846-5]
 - 11 **Campanacci M**. Bone and Soft Tissue Tumors. 2nd ed. Padova: Piccin Nuova Libraria, 1999: 54-56
 - 12 **Enneking WF**, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop Relat Res* 1980; (**153**): 106-120 [PMID: 7449206 DOI: 10.1097/00003086-198011000-00013]
 - 13 **Boriani S**, Weinstein JN, Biagini R. Primary bone tumors of the spine. Terminology and surgical staging. *Spine (Phila Pa 1976)* 1997; **22**: 1036-1044 [PMID: 9152458 DOI: 10.1097/00007632-199705010-00020]
 - 14 **Tokuhashi Y**, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine (Phila Pa 1976)* 2005; **30**: 2186-2191 [PMID: 16205345 DOI: 10.1097/01.brs.0000180401.06919.a5]
 - 15 **Tomita K**, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. *Spine (Phila Pa 1976)* 2001; **26**: 298-306 [PMID: 11224867 DOI: 10.1097/00007632-200102010-00016]
 - 16 **Tomita K**, Kawahara N, Baba H, Tsuchiya H, Fujita T, Toribatake Y. Total en bloc spondylectomy. A new surgical technique for primary malignant vertebral tumors. *Spine (Phila Pa 1976)* 1997; **22**: 324-333 [PMID: 9051895]
 - 17 **Campanacci M**. Bone and Soft Tissue Tumors. 2nd ed. Padova: Piccin Nuova Libraria, 1999: 58-63 [DOI: 10.1007/978-3-7091-3846-5]
 - 18 **Mavrogenis AF**, Papagelopoulos PJ, Soucacos PN. Skeletal osteochondromas revisited. *Orthopedics* 2008; **31** [PMID: 19226005]
 - 19 **Crist BD**, Lenke LG, Lewis S. Osteoid osteoma of the lumbar spine. A case report highlighting a novel reconstruction technique. *J Bone Joint Surg Am* 2005; **87**: 414-418 [PMID: 15687169 DOI: 10.2106/JBJS.C.01499]
 - 20 **Atesok KI**, Alman BA, Schemitsch EH, Peyser A, Mankin H. Osteoid osteoma and osteoblastoma. *J Am Acad Orthop Surg* 2011; **19**: 678-689 [PMID: 22052644]
 - 21 **Ofluoglu O**, Boriani S, Gasbarrini A, De Iure F, Donthineni R. Diagnosis and planning in the management of musculoskeletal tumors: surgical perspective. *Semin Intervent Radiol* 2010; **27**: 185-190 [PMID: 21629407 DOI: 10.1055/s-0030-1253516]
 - 22 **Yalniz E**, Ozcan M, Copuroglu C, Memisoglu S, Yalçin O. Osteosarcoma of the lumbar vertebra: case report and a review of the literature: rare localization with long survival. *Arch Orthop Trauma Surg* 2009; **129**: 1701-1705 [PMID: 19440724 DOI: 10.1007/s00402-009-0896-7]
 - 23 **Boriani S**, Bandiera S, Biagini R, Bacchini P, Boriani L, Cappuccio M, Chevalley F, Gasbarrini A, Picci P, Weinstein JN. Chordoma of the mobile spine: fifty years of experience. *Spine (Phila Pa 1976)* 2006; **31**: 493-503 [PMID: 16481964 DOI: 10.1097/BRS.0b013e31823d2143]

P- Reviewer: Anand A, Robertson GA **S- Editor:** Qiu S

L- Editor: Wang TQ **E- Editor:** Liu SQ



Basic Study

Effect of elbow position on radiographic measurements of radio-capitellar alignment

Emilie Sandman, Fanny Canet, Yvan Petit, G-Yves Laflamme, George S Athwal, Dominique M Rouleau

Emilie Sandman, Fanny Canet, Yvan Petit, G-Yves Laflamme, Dominique M Rouleau, Hôpital du Sacré-Cœur de Montréal, Montreal, Quebec H4J 1C5, Canada

George S Athwal, the Hand and Upper Limb Centre, Ontario N6A 4L6, Canada

Author contributions: Sandman E, Canet F and Rouleau DM performed the majority of experiments and analysed the data; Sandman E and Canet F performed the radiographic investigations; Petit Y, Athwal GS and Rouleau DM participated equally in the design of the research; all the authors contributed to the drafting of the paper.

Supported by Fondation de Recherche et d'Éducation en Orthopédie de Montréal.

Institutional review board statement: Comité d'éthique de la recherche de l'HSCM, CÉR 2010-04-32. Each individual was asked to give informed consent.

Informed consent statement: Each individual was asked to give informed consent.

Conflict-of-interest statement: The authors declare no conflicts of interest regarding this manuscript.

Data sharing statement: No data were created so no data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dominique M Rouleau, MD, MSc, FRCSC, Hôpital du Sacré-Cœur de Montréal, 5400 Boul Gouin O, Montreal, Quebec H4J 1C5, Canada. dominique.rouleau@umontreal.ca

Telephone: +1-514-3382222

Fax: +1-514-3383542

Received: May 15, 2015

Peer-review started: May 15, 2015

First decision: September 29, 2015

Revised: November 18, 2015

Accepted: December 3, 2015

Article in press: December 4, 2015

Published online: February 18, 2016

Abstract

AIM: To evaluate the effect of different elbow and forearm positions on radiocapitellar alignment.

METHODS: Fifty-one healthy volunteers were recruited and bilateral elbow radiographs were taken to form a radiologic database. Lateral elbow radiographs were taken with the elbow in five different positions: Maximal extension and forearm in neutral, maximal flexion and forearm in neutral, elbow at 90° and forearm in neutral, elbow at 90° and forearm in supination and elbow at 90° and forearm in pronation. A goniometer was used to verify the accuracy of the elbow's position for the radiographs at a 90° angle. The radiocapitellar ratio (RCR) measurements were then taken on the collected radiographs using the SliceOmatic software. An orthopedic resident performed the radiographic measurements on the 102 elbows, for a total of 510 lateral elbow radiographic measures. ANOVA paired *t*-tests and Pearson coefficients were used to assess the differences and correlations between the RCR in each position.

RESULTS: Mean RCR values were $-2\% \pm 7\%$ (maximal extension), $-5\% \pm 9\%$ (maximal flexion), and for elbow at 90° and forearm in neutral $-2\% \pm 5\%$, supination $1\% \pm 6\%$ and pronation $1\% \pm 5\%$. ANOVA analyses demonstrated significant differences between the RCR

in different elbow and forearm positions. Paired *t*-tests confirmed significant differences between the RCR at maximal flexion and flexion at 90°, and maximal extension and flexion. The Pearson coefficient showed significant correlations between the RCR with the elbow at 90° - maximal flexion; the forearm in neutral-supination; the forearm in neutral-pronation.

CONCLUSION: Overall, 95% of the RCR values are included in the normal range (obtained at 90° of flexion) and a value outside this range, in any position, should raise suspicion for instability.

Key words: Elbow subluxation; Radiocapitellar ratio; Elbow; Elbow dislocation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Assessing radial head alignment after injury and obtaining perfect lateral radiographs with the elbow at 90° and the forearm in neutral may be difficult. Therefore we designed this study to assess whether the radiocapitellar ratios (RCR) calculated from true lateral radiographs at different positions of elbow flexion and forearm pronosupination differ from those taken in 90° flexion and neutral position. The paper shows that the RCR measurement continues to be an overall valid and reliable method throughout different elbow and forearm positions. However, values in the negative range, > 5% regardless of forearm rotation, should raise suspicion for elbow instability.

Sandman E, Canet F, Petit Y, Laflamme GY, Athwal GS, Rouleau DM. Effect of elbow position on radiographic measurements of radio-capitellar alignment. *World J Orthop* 2016; 7(2): 117-122 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/117.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.117>

INTRODUCTION

The elbow is a complex joint that is comprised of three articulations: The ulno-humeral, the radiocapitellar and the proximal radio-ulnar joints. The joint capsule and the ligamentous structures surrounding the elbow's congruent osseous articulations provide static stability while its adjacent muscles and tendons offer dynamic stability by aligning and compressing the joint surfaces together^[1]. The components of elbow stability can be divided into primary and secondary stabilizers. The elbow's primary stabilizers consist of the anterior bundle of the medial collateral ligament, the lateral ulnar collateral ligament, and the ulnohumeral joint^[2]. The secondary stabilizers involve the radial head, the joint capsule and the adjacent muscles surrounding the articulation. All of these structures function together to permit functional elbow flexion-extension and forearm pronation-supination ranges of motion (ROM). However,

elbow stability and alignment can easily be disrupted after a trauma. In fact, the elbow is second only to the shoulder for the incidence of non-prosthetic joint dislocation^[3].

The literature highlights the importance of evaluating a joint's integrity throughout its full arc of movement, as the stability of an articulation is a dynamic process. Assessing an articulation with a single radiologic view may lead to suboptimal diagnostics and treatments. Therefore, the evaluation of the radiocapitellar joint, which is known to contribute to elbow stability, would be an added resource. In their study of 80 healthy elbows, Rouleau *et al*^[4] described a quantitative method to assess radiocapitellar joint translations, the radiocapitellar ratio (RCR), defined as the displacement of the radial head (minimal distance between the right bisector of the radial head and the center of the capitellum) divided by the diameter of the capitellum^[4]. The mean normal RCR was 4% ± 4% (95%CI: -5% to 13%). It has been reported to have good inter- and intra-observer reliability when measured on a lateral radiograph with the elbow positioned at 90° of flexion with neutral forearm rotation. In a trauma setting, it may be difficult to obtain standardized lateral radiographs with the elbow flexed at 90° and the forearm in neutral rotation due to factors such as pain, swelling, or fractures^[1], which may cause radiographs to be taken with the elbow and the forearm in different positions. The purpose of this study was to assess whether RCRs calculated from true lateral radiographs, at different positions of elbow flexion and forearm pronosupination, differ from those taken in 90° flexion and neutral position.

MATERIALS AND METHODS

Radiographs

Fifty-one healthy volunteers were recruited and bilateral elbow radiographs were taken to form a radiologic database. In this study, the volunteers included 31 females and 20 males, with an average age of 32 years old (SD = 9.0). The number of radiographs observed followed the guidelines of Harrison *et al*^[5]. The inclusion criteria were: patients aged between 18-50 years old, and the absence of a preexisting elbow pathology in both upper extremities. The exclusion criteria consisted of: Elbows with preexisting abnormalities, such as arthrosis, fractures, surgical implants, *etc.*, and pregnant women or those at risk of being pregnant. Each individual was asked to give informed consent and protected with lead aprons. They were asked to actively move their elbow into the various positions, so that no passive maximal pressure was applied. Ninety degree elbow flexion was assured by measuring with a goniometer at the time of imaging and was reviewed during measurements on the computer software. Lateral elbow radiographs were taken with the elbow in five different positions: Maximal extension and forearm in neutral, maximal flexion and forearm in neutral, elbow at 90° and forearm in neutral, elbow at 90° and forearm in supination and elbow at

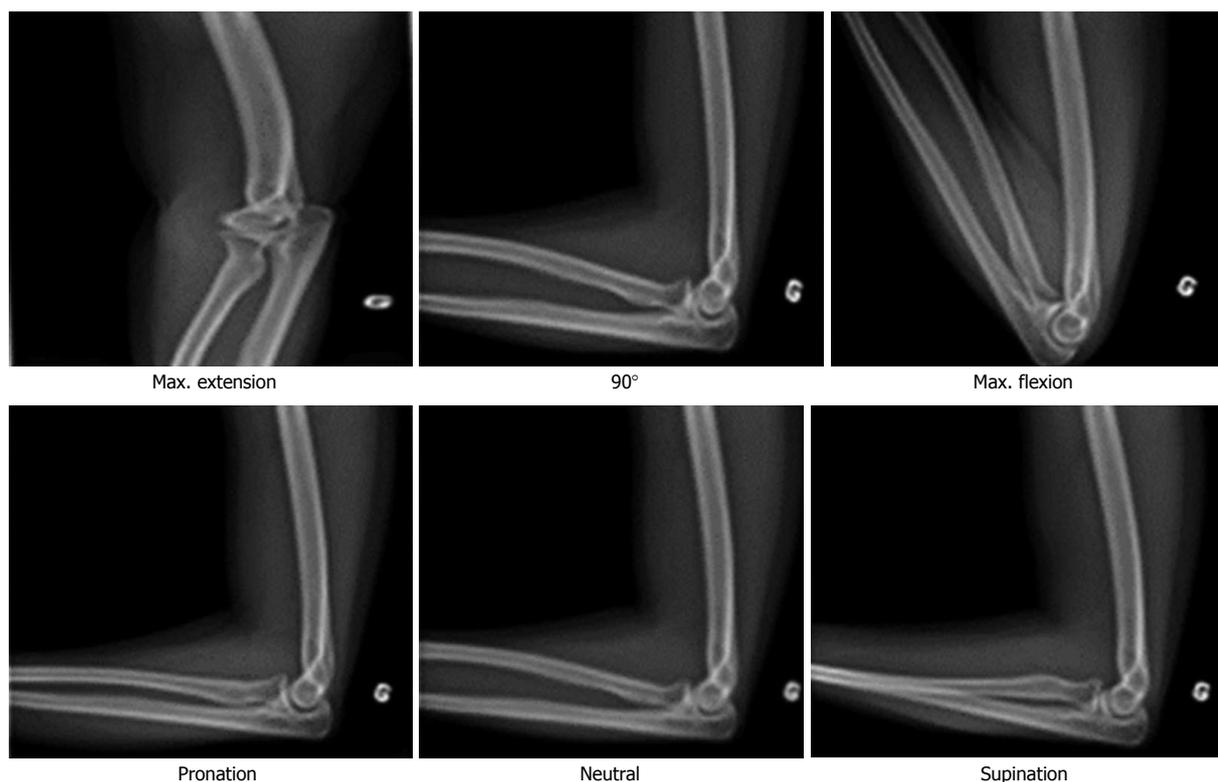


Figure 1 Different elbow and forearm positions evaluated.



Figure 2 Method for radiocapitellar ratio measurement. (1): A line, perpendicular to the joint, was drawn at the center of the articular surface of the radial head (point 1); (2): The diameter of the capitellum (\emptyset capitellum) was measured; (3): The center of the capitellum was identified as the bisector of the capitellum's diameter (point 2); (4): The minimal distance between the center points of the radial head and the capitellum was measured (D_{RH}); (5): The RCR was calculated: $RCR (\%) = D_{RH}/\emptyset_{capitellum}$. RCR: Radiocapitellar ratio.

90° and forearm in pronation (Figure 1). As described by London *et al.*^[4] a true lateral elbow radiograph was achieved when the trochlear sulcus, the capitellum and the medial trochlea were concentrically superimposed. The Institutional Review Board of the ethical committee approved this study.

Measurement method

The RCR method was used to measure the translation of the radial head on the capitellum, described in 5 steps^[4], with SliceOmatic (Tomovision Inc, Magog, Quebec,

Canada) software: (1) A line, perpendicular to the joint, was drawn at the center of the articular surface of the radial head (Figure 2, point 1); (2) The diameter of the capitellum (\emptyset capitellum) was measured; (3) The center of the capitellum was identified as the bisector of the capitellum's diameter (Figure 2); (4) The minimal distance between the center points of the radial head and the capitellum was measured (Figure 2); and (5) The Radiocapitellar-Ratio was calculated: $RCR (\%) = D_{RH}/\emptyset_{capitellum}$.

A positive RCR value indicates anterior radial head translation, while a negative RCR result signifies posterior radial head translation. An orthopedic resident (ES) performed the radiographic measurements on the 102 elbows, for a total of 510 lateral elbow radiographic measures. The intra-observer (0.72) and inter-observer reliability (0.52) of this method were previously reported using intraclass correlation tests^[4]. The results obtained were compared to the normal RCR range, measured in the previous study by Rouleau *et al.*^[4] and described as a RCR value between -5% to 13%. In their study, the measurements were taken twice by two different observers and the mean normal RCR was $4\% \pm 4\%$, with the normal RCR range within a 95%CI.

Statistical analysis

ANOVA and paired *t* tests were used to assess the differences in RCR measurement results between the five different elbow and forearm positions, with a level of significance established at $P < 0.05$. Pearson coefficients were calculated to assess the correlation between the

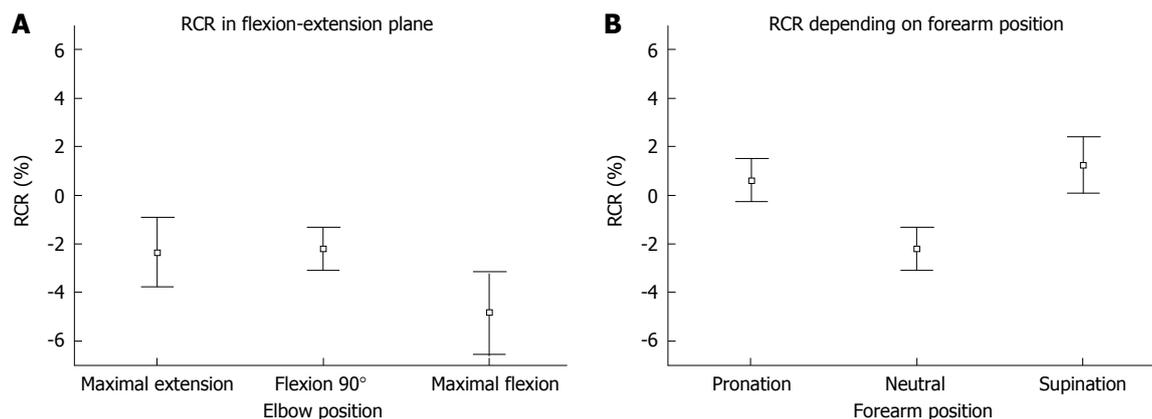


Figure 3 Mean radiocapitellar ratio and 95%CI for each elbow position (A) and prosupination movement (B). RCR: Radiocapitellar ratio.

Table 1 Paired *t*-tests for the different elbow and forearm positions

Paired <i>t</i> -test for elbow and forearm positions	<i>P</i>
Maximal elbow extension and maximal elbow flexion	0.034
Maximal elbow flexion and elbow flexion at 90°	0.003
Maximal elbow extension and elbow flexion at 90°	0.86
Forearm in neutral and forearm in pronation	0.001
Forearm in neutral and forearm in supination	0.001
Forearm in pronation and forearm in supination	0.28

RCR measurements in each different elbow and forearm position. Correlation coefficients (*r*) were considered small if $r = \pm 0.00$ to 0.09 ; medium if $r = \pm 0.10$ to 0.30 ; and strong if $r = \pm 0.50$ and 1.00 ^[7]. According to the results of the mean and standard deviation, analyses of the power for the Pearson coefficients correlations were also calculated. Statistical review of the study was performed by a biomedical statistician.

RESULTS

The mean maximal flexion achieved by the 51 subjects was of $151^\circ \pm 5^\circ$ and the mean maximal extension was of $12^\circ \pm 7^\circ$. The mean RCRs for each position were: elbow in maximal extension: $-2\% \pm 7\%$ (95%CI: -4% to -1%), elbow in maximal flexion: $-5\% \pm 9\%$ (95%CI: -6% to -3%), elbow at 90° and forearm in neutral: $-2\% \pm 5\%$ (95%CI: -3% to -1%), elbow at 90° and forearm in supination: $1\% \pm 6\%$ (95%CI: 0% to 2%), and elbow at 90° and forearm in pronation: $1\% \pm 5\%$ (95%CI: 0% to 2%) (Figure 3). According to the ANOVA results, a significant difference exists between the RCRs in different elbow positions ($P = 0.01$) and in different forearm positions ($P < 0.001$). Moreover, 95% of our cohort obtained RCR values between the normal ranges initially evaluated, with posterior translation of the radial head of 5% to anterior translation of 13%.

Paired *t* tests were used to accommodate the fact that these are non-independent events, and confirmed a significant difference between maximal elbow flexion and 90° of elbow flexion ($P = 0.003$), as well as for maximal elbow extension and maximal elbow flexion

($P = 0.034$) (Table 1). Additionally, the paired *t* test showed significant differences between the positions of the forearm in neutral and pronation ($P \leq 0.001$), as well as between the forearm in neutral and supination ($P < 0.001$). However, there was no significant difference between the positions of elbow flexion at 90° and maximal extension ($P = 0.86$), nor between the positions of the forearm in pronation and in supination ($P = 0.28$).

According to the Pearson coefficients, significant correlations exist between elbow flexion at 90° and in maximal flexion ($r = 0.19$, $P = 0.049$), the forearm in neutral and in supination ($r = 0.34$, $P < 0.001$), as well as the forearm in neutral and in pronation ($r = 0.42$, $P < 0.001$).

There was no significant correlation observed between the forearm positions in pronation and supination ($r = 0.37$, $P = 0.55$), the elbow positioned at 90° and in maximal extension ($r = 0.086$, $P = 0.39$) or between maximal elbow flexion and maximal elbow extension ($r = 0.085$, $P = 0.39$).

Post hoc power analyses of the Pearson coefficient correlations were done for the different elbow and forearm positions (Table 2). Significant power was only obtained when comparing maximal elbow flexion and maximal elbow extension ($\Pi = 0.84$). The power calculated for elbow flexion at 90° with the forearm in neutral and maximal elbow extension was $\Pi = 0.63$, and $\Pi = 0.05$ for elbow flexion at 90° with the forearm in neutral and maximal elbow flexion. When analyzing the power for the different forearm positions, significant results were obtained when comparing pronation and neutral, as well as between supination and neutral forearm positions, both with a power $\Pi = 0.99$. The power found for the correlation between supination and pronation forearm positions was 0.18.

DISCUSSION

Following upper extremity trauma, a complete evaluation of the elbow's primary and secondary stabilizers is necessary to avoid occult injuries and inappropriate treatments. The stability of an articulation can be

Table 2 Pearson coefficient correlation power analyses for the different elbow positions and forearm positions

	<i>r</i>	<i>P</i>	Power (Π)
Pearson coefficient correlation for the elbow			
Maximal extension and Maximal flexion	-0.0854	0.394	0.84
Maximal flexion and flexion at 90°	0.1948	0.050	0.05
Maximal extension and flexion at 90°	-0.0860	0.390	0.63
Pearson coefficient correlation for the forearm			
Neutral and pronation	0.42	0.001	0.99
Neutral and supination	0.34	0.001	0.99
Pronation and supination	0.37	0.55	0.18

determined clinically or with radiographic imaging. In the trauma setting, an elbow's clinical stability and complete ROM evaluation may be difficult due to associated injuries and pain. Perfect lateral radiologic views at 90° of flexion may also be difficult to obtain due to multiple factors. Cheung *et al*^[8] described the importance of obtaining proper alignment on a lateral radiograph with the forearm in neutral, with views of both the elbow and the wrist. Moreover, it has been suggested in the literature that stability of the radial head, especially after reduction, should be evaluated throughout its full ROM under radiological imaging which is what would make the RCR value of interest.

When analyzing the results obtained with the paired *t*-tests, significant differences were found for the RCR measurements between maximal elbow flexion and elbow flexion at 90°; between maximal elbow flexion and maximal elbow extension; between neutral and pronation forearm positions; as well as between neutral and supination forearm positions. Thus, elbow and forearm positioning seem to substantially influence radiocapitellar alignment, because our results tend to demonstrate significant differences for most of the positions evaluated. Although these differences are statistically significant, further research is needed to evaluate if they are clinically important, as a RCR of 5% represents a small translation of the radial head (1.25 mm for a capitellum of 25 mm of diameter).

The RCR measurement method has previously been shown to be valid and reliable when evaluating translations of the radiocapitellar articulation, with the elbow at 90° and the forearm in neutral^[4]. This study evaluated the RCR method in five different elbow and forearm positions. The different elbow positions seem to have a greater effect on the RCR measurement results, when compared to the different forearm ranges of motion. Nonetheless, 95% of our cohort obtained RCR values between the normal ranges initially evaluated from -5% to 13%^[4]. To illustrate, this range corresponds, in a capitellum with a diameter of 25 mm, to a radiocapitellar translation of 1.25 mm posterior to 3.25 mm anterior, for a total average of 5 mm displacement. Thus, the RCR measurement continues to be an overall valid and reliable method throughout different elbow and forearm positions.

The main limitations of this study are that the radiographs were all taken with the radiological beam perpen-

dicular to the elbow joint, to obtain a perfect lateral view. Further studies should be done to evaluate the effect of the radiological beam angle on the measurement of radial head displacement, since radiographs taken with mild misalignment or with the elbow slightly oblique might influence the measurements. Finally, an injured elbow may not be able to achieve the different elbow positions tested in the study, due to pain, swelling or altered mechanics. However, the positions were chosen to cover the entire range of motion of the elbow, as well as to maximize the differences on the RCR measurements.

To conclude, even if positioning is not ideal, if a true lateral radiograph of the elbow is taken, the RCR should fall within the normal range of -5% to 13% when the radiocapitellar joint is intact. The RCR measurement method is dependent on elbow (flexion-extension) and forearm (pronation-supination) positions. In both maximal elbow positions in flexion and extension, the measurements of the RCR have a higher standard deviation. In order to decrease its variability, we recommend, as a convention, measuring the RCR on lateral radiographs with the elbow at 90° and the forearm in any position (pronation, neutral or supination). In normal elbows, at 90° of flexion, the RCR measurement with the forearm in pronation and supination show a significant difference from the forearm in neutral, and move the RCR in a positive direction. Therefore values in the negative range, > 5% regardless of forearm rotation, should raise suspicion for instability. A clinical study on the prognosis value of RCR in the presence of acute elbow dislocation would further support its clinical utility^[9].

COMMENTS

Background

The elbow is a complex joint that is comprised of three articulations and all of these structures function together to permit functional elbow flexion-extension and forearm pronation-supination ranges of motion (ROM). The literature highlights the importance of evaluating a joint's integrity throughout its full arc of movement, since the stability of an articulation is a dynamic process. However, elbow stability and alignment can easily be disrupted after a trauma and few reliable measurement methods are available. The radiocapitellar ratio (RCR) was described as a quantitative method to assess radiocapitellar joint translation on standardized lateral radiographs with the elbow flexed at 90° and the forearm in neutral rotation. However, it may be difficult in a trauma setting to obtain perfect lateral radiographs. Thus, it was of interest to assess whether the RCRs calculated from true lateral radiographs, at different positions of elbow flexion and forearm pronation-supination, differ from those taken in 90° flexion and neutral position.

Research frontiers

The authors aimed to evaluate the effect of different elbow and forearm positions on radiocapitellar alignment, using the RCR on fifty-one healthy volunteers. Bilateral elbow radiographs were taken with the elbow in five different positions to form a radiologic database to investigate if elbow position influenced the RCR.

Innovations and breakthroughs

This study demonstrate that even if positioning is not ideal, if a true lateral radiograph of the elbow is taken, the RCR should fall within the normal range of -5% to 13% when the radiocapitellar joint is intact. However, values in the negative range, > 5% regardless of forearm rotation, should raise suspicion for elbow instability or subluxation.

Applications

The authors believe that further studies should be done to evaluate the effect of the radiological beam angle on the measurement of radial head displacement, since radiographs taken with mild misalignment or with the elbow slightly oblique might influence the measurements.

Terminology

A quantitative method to assess radiocapitellar joint translations, the RCR, is defined as the displacement of the radial head (minimal distance between the right bisector of the radial head and the center of the capitellum) divided by the diameter of the capitellum. The mean normal RCR is $4\% \pm 4\%$ (95%CI: -5% to 13%). It has been reported to have good inter- and intra-observer reliability when measured on a lateral radiograph with the elbow positioned at 90 degrees of flexion with neutral forearm rotation.

Peer-review

The authors concur with the literature with regard to the importance of obtaining proper alignment on a lateral radiograph with the forearm in neutral, with views of both the elbow and the wrist. Moreover, stability of the radial head, especially after reduction, should be evaluated throughout its full ROM under radiological imaging which is what would make the RCR value of interest. Therefore, this review article may have potential to increase knowledge to optimize diagnosis and treatment of elbow injuries.

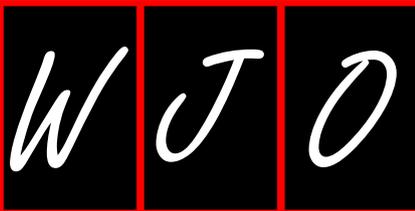
REFERENCES

1 **Herman MJ**, Boardman MJ, Hoover JR, Chafetz RS. Relationship

- of the anterior humeral line to the capitellar ossific nucleus: variability with age. *J Bone Joint Surg Am* 2009; **91**: 2188-2193 [PMID: 19723996 DOI: 10.2106/JBJS.H.01316]
- 2 **Athwal GS**, Ramsey ML, Steinmann SP, Wolf JM. Fractures and dislocations of the elbow: a return to the basics. *Instr Course Lect* 2011; **60**: 199-214 [PMID: 21553774]
- 3 **Coonrad RW**, Roush TF, Major NM, Basamania CJ. The drop sign, a radiographic warning sign of elbow instability. *J Shoulder Elbow Surg* 2005; **14**: 312-317 [PMID: 15889032]
- 4 **Rouleau DM**, Sandman E, Canet F, Djahangiri A, Laflamme Y, Athwal GS, Petit Y. Radial head translation measurement in healthy individuals: the radiocapitellar ratio. *J Shoulder Elbow Surg* 2012; **21**: 574-579 [PMID: 21724422 DOI: 10.1016/j.jse.2011.03.017]
- 5 **Harrison DE**, Harrison DD, Cailliet R, Janik TJ, Holland B. Radiographic analysis of lumbar lordosis: centroid, Cobb, TRALL, and Harrison posterior tangent methods. *Spine (Phila Pa 1976)* 2001; **26**: E235-E242 [PMID: 11389407]
- 6 **London JT**. Kinematics of the elbow. *J Bone Joint Surg Am* 1981; **63**: 529-535 [PMID: 7217119]
- 7 **Cohen J**. Statistical Power Analysis for the Behavioral Sciences, 2nd edition. NY, New York: Routledge Academic, 1988
- 8 **Cheung EV**, Yao J. Monteggia fracture-dislocation associated with proximal and distal radioulnar joint instability. A case report. *J Bone Joint Surg Am* 2009; **91**: 950-954 [PMID: 19339581 DOI: 10.2106/JBJS.H.00269]
- 9 **Windisch G**, Clement H, Grechenig W, Tesch NP, Pichler W. The anatomy of the proximal ulna. *J Shoulder Elbow Surg* 2007; **16**: 661-666 [PMID: 17531510]

P- Reviewer: Malik H, Ranjan Patra S **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Liu SQ





Prospective Study

Reverse-total shoulder arthroplasty cost-effectiveness: A quality-adjusted life years comparison with total hip arthroplasty

Daniel Bachman, John Nyland, Ryan Krupp

Daniel Bachman, John Nyland, Ryan Krupp, Department of Orthopaedic Surgery, University of Louisville, Louisville, KY 40202, United States

John Nyland, Athletic Training Program, Kosair Charities College of Health and Natural Sciences, Spalding University, Louisville, KY 40203, United States

Ryan Krupp, Norton Orthopaedic and Sports, Louisville, KY 40241, United States

Author contributions: Bachman D drafted the manuscript and performed data analysis; Nyland J participated in study design and edited the manuscript; Krupp R provided oversight to manuscript development, recruited patients, and collected data; all authors read and approved the final manuscript.

Institutional review board statement: This study was approved by the University of Louisville and Norton Healthcare Medical Institutional Review Boards (NHORA 12-No155).

Clinical trial registration statement: Data used in this study was obtained from clinical trial PS-901.

Informed consent statement: All study participants provided written consent prior to study enrollment.

Conflict-of-interest statement: Dr. Ryan Krupp has served as a past consultant for DJO Surgical previously receiving an honorarium for teaching and also for research support. Drs. Bachman and Nyland have no conflicts of interest to disclose.

Data sharing statement: There is no additional data available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: John Nyland, Director, Professor, Athletic Training Program, Kosair Charities College of Health and Natural Sciences, Spalding University, 901 South 3rd Street, Louisville, KY 40203, United States. jnyland@spalding.edu
Telephone: +1-502-8734224
Fax: +1-502-5857149

Received: July 3, 2015

Peer-review started: July 9, 2015

First decision: September 30, 2015

Revised: October 10, 2015

Accepted: December 7, 2015

Article in press: December 8, 2015

Published online: February 18, 2016

Abstract

AIM: To compare reverse-total shoulder arthroplasty (RSA) cost-effectiveness with total hip arthroplasty cost-effectiveness.

METHODS: This study used a stochastic model and decision-making algorithm to compare the cost-effectiveness of RSA and total hip arthroplasty. Fifteen patients underwent pre-operative, and 3, 6, and 12 mo post-operative clinical examinations and Short Form-36 Health Survey completion. Short form-36 Health Survey subscale scores were converted to EuroQual Group Five Dimension Health Outcome scores and compared with historical data from age-matched patients who had undergone total hip arthroplasty. Quality-adjusted life year (QALY) improvements based on life expectancies were calculated.

RESULTS: The cost/QALY was \$3900 for total hip arthroplasty and \$11100 for RSA. After adjusting the model to only include shoulder-specific physical function subscale items, the RSA QALY improved to 2.8

years, and its cost/QALY decreased to \$8100.

CONCLUSION: Based on industry accepted standards, cost/QALY estimates supported both RSA and total hip arthroplasty cost-effectiveness. Although total hip arthroplasty remains the quality of life improvement “gold standard” among arthroplasty procedures, cost/QALY estimates identified in this study support the growing use of RSA to improve patient quality of life.

Key words: Quality of life; Arthroplasty; Shoulder; Cost-analysis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Based on industry accepted standards, cost/quality-adjusted life year (QALY) estimates supported both reverse-total shoulder arthroplasty (RSA) and total hip arthroplasty cost-effectiveness. The cost/QALY estimates identified in this study support the growing use of RSA to improve patient quality of life.

Bachman D, Nyland J, Krupp R. Reverse-total shoulder arthroplasty cost-effectiveness: A quality-adjusted life years comparison with total hip arthroplasty. *World J Orthop* 2016; 7(2): 123-127 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/123.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.123>

INTRODUCTION

The biomechanical advantage provided by improved deltoid muscle function following reverse-total shoulder arthroplasty (RSA) has led to its increased use for treating patients with massive rotator cuff tear arthropathy, severe shoulder fracture or gleno-humeral joint degeneration. Associated with this increased use is the need to better identify RSA cost-effectiveness with consideration for revision challenges^[1], and its true utility in the context of diminishing healthcare financial resources^[2]. History has demonstrated that total hip and knee arthroplasty use has progressively increased among patients with widely-ranging ages and diagnoses^[3,4]. If patient outcomes prove comparable to these other arthroplasty procedures a similar evolution may develop for RSA.

The cost-effectiveness of RSA in terms of quality-adjusted life years (QALY) within the context of healthcare industry standards is currently unknown^[5]. The purpose of this study was to compare RSA cost-effectiveness with total hip arthroplasty cost-effectiveness, widely considered to be the “gold standard” among arthroplasty procedures^[6]. The study hypothesis was that both procedures would prove cost effective based on industry accepted standards of a \$30000-50000 dollars United States/QALY^[1-4]. Information such as this would provide vital insight into the true efficacy of RSA.

MATERIALS AND METHODS

Following University of Louisville and Norton Healthcare Medical Institutional Review Board approvals, 15 consecutive patients preparing to undergo RSA underwent pre-operative clinical examination by the same fellowship-trained shoulder surgeon. All patients had severe rotator cuff arthropathy. Given the lack of functional rotator cuff tissue an RSA was selected rather than a standard total shoulder arthroplasty. By reversing humeral head and glenoid component locations, RSA increased deltoid muscle mechanical efficiency during shoulder elevation and improved joint stability. All patients received a Donjoy Orthopaedic Reverse Shoulder Prosthesis (DJO, Vista, CA, United States). Patients also completed the short form-36 Health Survey subscales [physical function (PF), role physical (RP), role emotional (RE), bodily pain (BP), general health (GH), vitality (VT), mental health (MH), and social function (SF)]. Clinical examination and short form-36 surveys were repeated at 3-mo, 6-mo, and at 1-year post-surgery. By the end of the first post-operative year all patients were satisfied with the RSA procedure and had met their pain reduction and functional restoration expectations. These data were compared with the findings of Mangione *et al*^[7] who studied 224 patients of similar age following total hip arthroplasty over the same follow-up time intervals, also collecting 0-100 point scale short form-36 survey data. Short form-36 subscale data from both studies was converted to EuroQual Group Five Dimension Health Outcome Scores using previously reported methods^[8] and the following formula ($\alpha \times PF + \beta \times RP + \gamma \times RE + \delta \times BP + \varepsilon \times GH + \zeta \times VT + \eta \times MH + \theta \times SF$). In this formula the Greek letters signify constants from an accepted conversion algorithm^[8]. Short form-36 physical function subscale score values for each follow-up time period were converted to QALY values^[8]. Baseline values were then subtracted from follow-up QALY scores to identify condition improvements over time (1, 6 and 12 mo). This accounted for the entire first post-surgical year. For study purposes a 12 mo follow-up period was considered representative of peak quality of life improvement following arthroplasty^[9,10].

A stochastic model and decision making algorithm^[11,12] (Figure 1) incorporated revision rates^[13,14] and a standard annual general health reduction to incrementally estimate QALY changes from baseline for each arthroplasty procedure simulating aging over the course of life expectancy^[12]. The expected revision rate for each procedure (revisions/patient years followed) was applied to the stochastic model (Ω_1, Ω_2). Patient revisions/patient years was determined by taking the estimated number of procedural revisions divided by the number of patient follow-up years for total hip^[13] and RSA^[14]. For the duration of stochastic model application, for a projected revision, then the remainder of projected quality of life was considered to be only 50% improved from baseline state. If the patient required revision surgery 50% of their QALY potential was decreased

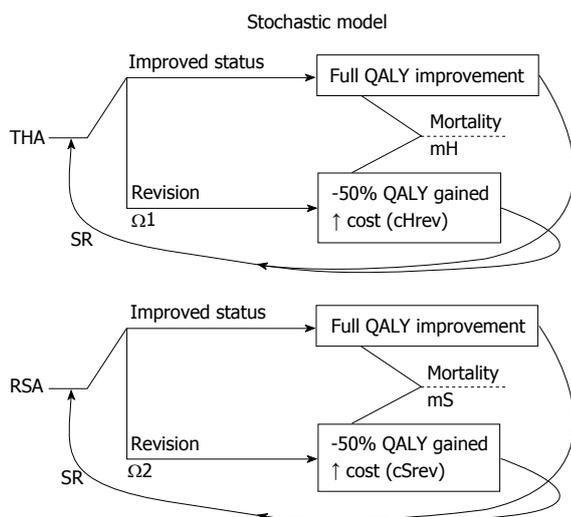


Figure 1 Stochastic model and decision-making algorithm. RSA: Reverse-total shoulder arthroplasty; QALY: Quality-adjusted life year; THA: Total hip arthroplasty; SR: Standard reduction in quality of life.

from that point forward^[15]. A 3% annual general health decline representative of aging was also added to the model^[16]. Annual quality of life improvement represented the previous year's quality of life improvement over baseline minus revision rate and standard general health reduction (3%). Collective quality of life improvement over baseline values were summed for the years of projected life for each arthroplasty group. This represented the QALY associated with each arthroplasty procedure.

Stochastic model variable definitions are provided in Table 1. Pre- (Hpreop, Rpreop) and post-operative (Ipostop) costs for each arthroplasty method including implant costs and hospital associated direct costs were determined using previously reported data^[9] and data obtained from the hospital where the surgical procedure was performed. The same preoperative assessments were assumed for both arthroplasty surgical groups^[9]. The average cost of a revision (Hrev or Rrev) was calculated by summing the non-implant related surgical and hospital costs (Hsurg or Rsurg), and the cost of the revised implant components (Hrevimplant or Rrevimplant), based on historical data^[13,14] and post-operative cost estimates^[15]. Revision costs calculated by the model represented the proportion of patients expected to undergo a revision multiplied by the average cost of a revision (either Hrev or Rrev). Revision expenses were then added to the primary cost. Cost per QALY were then calculated for each procedure.

Further evaluation was performed to determine the influence of short form-36 Health Survey subscale scores on the QALY of patients following total hip arthroplasty and RSA. Similar to the report of March *et al.*^[17], pain, physical function, and role-physical subscale scores displayed the greatest influence on QALY score improvement following either surgical procedure. The strongest single influence on QALY score improvement for both total hip arthroplasty and RSA was the physical

function subscale. Focused attention to this subscale revealed that of 10 total items, nine related more specifically to ambulation while only three related more specifically to shoulder function. These included item 3a moderate activities such as moving a table, pushing a vacuum cleaner, bowling, or playing golf; item 3c lifting or carrying groceries; and item 3j bathing or dressing yourself^[18]. The stochastic model was used to calculate QALY using both aggregate physical function subscale scores and scores based solely on the three more shoulder-specific physical function subscale question items.

RESULTS

Estimated QALY values were 2.0 years for RSA and 3.5 years for total hip arthroplasty. When the stochastic model and decision-making algorithm was applied without standard reductions for revision rates QALY values improved to 2.8 years for RSA and to 4.7 years for total hip arthroplasty. Total direct and indirect hospital cost estimates were \$17000 for RSA and \$11700 for total hip arthroplasty. Costs increased to \$22200 and \$13800, respectively, when adjusted for revision. Using these calculations the cost/QALY was \$11100 for RSA and \$3900 for total hip arthroplasty. Primary and revision implant costs represented 58% of RSA and 43% of total hip arthroplasty costs.

Short form-36 Health Survey physical function subscale scores initially revealed a considerable QALY value disparity between RSA and total hip arthroplasty patient groups. However, when including only shoulder-specific short form-36 physical function questions RSA QALY scores improved from 2.0 to 2.8 (*t*-test, *P* = 0.01) and RSA cost/QALY decreased to \$8100.

DISCUSSION

The most important study finding is that the cost/QALY score for RSA is considerably less than the industry accepted standard of \$30000-50000 cost/QALY^[1-4]. Since only 3 of 10 (30%) short form-36 physical function subscale questions are specific to upper extremity function; this subscale is naturally skewed toward a hip and locomotion focus. When considering solely more shoulder-specific physical function subscale items the RSA QALY score improved significantly and shoulder region-specific estimate validity also improved.

Using a similar stochastic model and decision-making algorithm, Coe *et al.*^[5] reported that an implant cost less than \$7000 United States dollars would make the RSA slightly more efficacious than shoulder hemiarthroplasty. In our study, total hip arthroplasty was approximately 2-3 times more cost effective than RSA. This finding however, does not preclude RSA cost effectiveness based on current industry accepted standards^[1-4]. In a prospective study of 55 patients who were 70.8 (range = 46-88 years) years of age at time of RSA, Virani *et al.*^[2] reported that at a mean 48 mo

Table 1 Markov stochastic model

Component	Abbreviation	Value
Age of THA patients, yr ± SD ^[7]	AgeH	67.9 ± 9.0
Gender of THA patients, % men, % women ^[7]	%H-M, %H-W	46%, 54%
Age of RSA patient, yr ± SD	AgeS	69.3 ± 7.7
Gender of reverse shoulder patients, % men, % women	%RSM, %RSW	60%, 40%
Standard reduction in quality of life ^[9]	SR	-3%
¹ Pre-operative THA cost, \$ ^[7]	Hpreop	400
¹ Pre-operative RSA cost, \$ ^[2]	Rpreop	600
¹ Cost of THA implant, \$	Himplant	4300
¹ THA surgical and hospital costs, \$	Hsurg	5600
¹ Total direct cost of THA, \$	dcTHA	Himplant + Hsurg = 9900
¹ Cost of post-operative implant care, \$ ^[7]	Ipostop	1400
¹ Cost of primary THA, \$	cTHA	dcTHA + Hpreop + Ipostop = 11700
Cost of THA revision implant, \$ ^[13]	Hrevimplant	%cup × cCup + %liner × cLiner + %stem × cStem = 1700
Average cost of THA revision, \$ ^[13]	Hrev	Hsurg + Hrevimplant = 7300
¹ Cost of RSA implant, \$	Rimplant	8900
¹ RSA surgical, hospital costs, \$	Rsurg	6100
¹ Total direct primary RSA cost, \$	dcRSA	Rimplant + Rsurg = 15000
¹ Primary RSA cost, \$	cRSA	dcRSA + Rpreop + Ipostop = 17000
¹ RSA revision implant cost, \$	Rrevimplant	%glenoid × cGS + %Stem × cStem + %poly × cPoly %Hemi × cHemi = 4000
¹ Average revision RSA cost, \$	Rrev	Rsurg + Rrevimplant
The length of first, second, third cycles hip, yr	hCL1, hCL2, hCL3	0.083, 0.416, 0.5
The length of first, second, third cycles shoulder, yr	sCL1, sCL2, sCL3	0.25, 0.25, 0.5
Length of cycle thereafter both, yr	CL	1
Age-specific mortality rate male, female ^[12]	mAgeM, AgeF	2007 United States life tables
Mortality rate, shoulder	mS	mAgeM × %SM + mAgeF × %SF
Mortality rate, hip	mH	mAgeM × %HM + mAgeF × %HF
THA revision cases ^[13]	hRev	44
Published cases ^[13]	hPC	211
THA follow-up years ^[13]	hFY	13.9 × hPC = 2932
Probability of THA revision/shoulder, yr	Ω1	hRev/hFY = 0.015
RSA revisions ^[14]	sRev	79
Published cases ^[14]	sPC	782
RSA follow-up years ^[14]	sFY	3.5 × sPC = 2737
RSA revision probability per shoulder, yr	Ω2	sRev/sFY = 0.029
Utility, quality of life improvement, EQ-5D	pQoL, oQoL	$\alpha \times PF + \beta \times RP + \gamma \times RE + \delta \times BP + \epsilon \times GH + \zeta \times VT + \eta \times MH + \theta \times SF$
Utility hip, shoulder	qHwell, qSwell	oQOL - pQOL
The utility associated with a THA revision, QALY	qHrev	0.5 × qHwell
The utility associated with a RSA revision, QALY	qSrev	0.5 × qSwell

¹Norton Healthcare cost data Louisville, KY, United States. RSA: Reverse-total shoulder arthroplasty; QALY: Quality-adjusted life year; THA: Total hip arthroplasty; PF: Physical function; RP: Role physical; RE: Role emotional; BP: Bodily pain; GH: General health; VT: Vitality; MH: Mental health; SF: Social function; oQOL: Post-operative quality of life; pQOL: Pre-operative quality of life.

follow-up patients had an 82% shoulder pain reduction and a 70% shoulder function improvement. This study estimated a mean 4-year total cost of \$24661, with hospitalization accounting for 92% of the total cost^[2]. These findings suggest the need for an earlier transition to a less expensive outpatient care environment as an important step in managing post-RSA costs.

Study limitations

The small sample size of this study necessitated several stochastic modeling assumptions. With the development of more shoulder-specific quality of life measurement tools and additional long-term RSA revision rate data, cost effectiveness estimates will become more accurate^[5]. Regardless, identical analytical procedures were performed for both arthroplasty patient groups generating valid, cost/QALY estimates. Since patient outcomes, hospitalization timetables, and implant costs may be influenced by multiple factors including regional

differences, patient age and comorbidities, rehabilitation strategies and activity expectations, clinicians are advised to use care when extrapolating these data to individual practice sites.

Conclusion

Based on industry accepted standards, cost/QALY estimates supported both RSA and total hip arthroplasty cost-effectiveness. Although total hip arthroplasty remains the quality of life improvement “gold standard” among arthroplasty procedures, cost/QALY estimates identified in this study support the growing use of RSA to improve patient quality of life.

COMMENTS

Background

Comparing the reverse-total shoulder arthroplasty (RSA) with the “gold standard” arthroplasty procedure was a daunting task.

Research frontiers

The results of this study confirm the efficacy of RSA for positively impacting patient quality of life.

Innovations and breakthroughs

Since hospitalization accounted for a high percentage of the total cost, future studies should investigate the efficacy of making an earlier transition to a less expensive outpatient care environment.

Peer-review

This is a nice paper.

REFERENCES

- 1 **Boileau P**, Melis B, Duperron D, Moineau G, Rumian AP, Han Y. Revision surgery of reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2013; **22**: 1359-1370 [PMID: 23706884 DOI: 10.1016/j.jse.2013.02.004]
- 2 **Virani NA**, Williams CD, Clark R, Polikandriotis J, Downes KL, Frankle MA. Preparing for the bundled-payment initiative: the cost and clinical outcomes of reverse shoulder arthroplasty for the surgical treatment of advanced rotator cuff deficiency at an average 4-year follow-up. *J Shoulder Elbow Surg* 2013; **22**: 1612-1622 [PMID: 23566674 DOI: 10.1016/j.jse.2013.01.003]
- 3 **Sharkey PF**, Austin MS, Hozack W. Total hip arthroplasty in the young patient. *Instr Course Lect* 2006; **55**: 173-176 [PMID: 16958450 DOI: 10.1053/j.sart.2004.12.021]
- 4 **Engh GA**. Advances in knee arthroplasty for younger patients: traditional knee arthroplasty is prologue, the future for knee arthroplasty is prescient. *Orthopedics* 2007; **30**: 55-57 [PMID: 17824335]
- 5 **Coe MP**, Greiwe RM, Joshi R, Snyder BM, Simpson L, Tosteson AN, Ahmad CS, Levine WN, Bell JE. The cost-effectiveness of reverse total shoulder arthroplasty compared with hemiarthroplasty for rotator cuff tear arthropathy. *J Shoulder Elbow Surg* 2012; **21**: 1278-1288 [PMID: 22265767 DOI: 10.1016/j.jse.2011.10.010]
- 6 **Räsänen P**, Paavolainen P, Sintonen H, Koivisto AM, Blom M, Ryyänänen OP, Roine RP. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. *Acta Orthop* 2007; **78**: 108-115 [PMID: 17453401 DOI: 10.1080/17453670610013501]
- 7 **Mangione CM**, Goldman L, Orav EJ, Marcantonio ER, Pedan A, Ludwig LE, Donaldson MC, Sugarbaker DJ, Poss R, Lee TH. Health-related quality of life after elective surgery: measurement of longitudinal changes. *J Gen Intern Med* 1997; **12**: 686-697 [PMID: 9383137 DOI: 10.1046/j.1525-1497.1997.07142.x]
- 8 **Ara R**, Brazier J. Deriving an algorithm to convert the eight mean SF-36 dimension scores into a mean EQ-5D preference-based score from published studies (where patient level data are not available). *Value Health* 2008; **11**: 1131-1143 [PMID: 18489495 DOI: 10.1111/j.1524-4733.2008.00352.x]
- 9 **Rissanen P**, Aro S, Sintonen H, Slätis P, Paavolainen P. Quality of life and functional ability in hip and knee replacements: a prospective study. *Qual Life Res* 1996; **5**: 56-64 [PMID: 8901367 DOI: 10.1007/bf00435969]
- 10 **Nilsdotter AK**, Lohmander LS. Patient relevant outcomes after total hip replacement. A comparison between different surgical techniques. *Health Qual Life Outcomes* 2003; **1**: 21 [PMID: 12816544]
- 11 **Hazen GB**. Stochastic trees: a new technique for temporal medical decision modeling. *Med Decis Making* 1992; **12**: 163-178 [PMID: 1513207 DOI: 10.1177/0272989x9201200302]
- 12 **Heron M**, Hoyert DL, Murphy SL, Xu J, Kochanek KD, Tejada-Vera B. Deaths: final data for 2006. *Natl Vital Stat Rep* 2009; **57**: 1-134 [PMID: 19788058]
- 13 **Engh CA**, Claus AM, Hopper RH, Engh CA. Long-term results using the anatomic medullary locking hip prosthesis. *Clin Orthop Relat Res* 2001; **(393)**: 137-146 [PMID: 11764343 DOI: 10.1097/0003086-200112000-00016]
- 14 **Zumstein MA**, Pinedo M, Old J, Boileau P. Problems, complications, reoperations, and revisions in reverse total shoulder arthroplasty: a systematic review. *J Shoulder Elbow Surg* 2011; **20**: 146-157 [PMID: 21134666 DOI: 10.1016/j.jse.2010.08.001]
- 15 **Dawson J**, Fitzpatrick R, Murray D, Carr A. Comparison of measures to assess outcomes in total hip replacement surgery. *Qual Health Care* 1996; **5**: 81-88 [PMID: 10158596 DOI: 10.1136/qshc.5.2.81]
- 16 **Siegel JE**, Torrance GW, Russell LB, Luce BR, Weinstein MC, Gold MR. Guidelines for pharmacoeconomic studies. Recommendations from the panel on cost effectiveness in health and medicine. Panel on cost Effectiveness in Health and Medicine. *Pharmacoeconomics* 1997; **11**: 159-168 [PMID: 10172935 DOI: 10.2165/00019053-199711020-00005]
- 17 **March LM**, Cross MJ, Lapsley H, Brnabic AJ, Tribe KL, Bachmeier CJ, Courtenay BG, Brooks PM. Outcomes after hip or knee replacement surgery for osteoarthritis. A prospective cohort study comparing patients' quality of life before and after surgery with age-related population norms. *Med J Aust* 1999; **171**: 235-238 [PMID: 10495753]
- 18 **Ware JE**, Snow KK, Kosinski M. SF-36® Health Survey: Manual and Interpretation Guide. Lincoln, RI: QualityMetric Incorporated, 2000

P- Reviewer: Fenichel I, Hasegawa M **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Liu SQ



Corrective osteotomies of the radius: Grafting or not?

Raffaele Mugnai, Luigi Tarallo, Enrico Lancellotti, Francesco Zambianchi, Ettore Di Giovine, Fabio Catani, Roberto Adani

Raffaele Mugnai, Luigi Tarallo, Enrico Lancellotti, Francesco Zambianchi, Ettore Di Giovine, Fabio Catani, Orthopedics and Traumatology Department, Modena Policlinic, University of Modena and Reggio Emilia, 41124 Modena, Italy

Roberto Adani, Department of Hand Surgery and Microsurgery, University Hospital Policlinico di Modena, 41124 Modena, Italy

Author contributions: Mugnai R, Catani F and Adani R designed the research; Lancellotti E and Di Giovine E performed the research; Mugnai R, Tarallo L and Zambianchi F wrote the paper.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest concerning this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Raffaele Mugnai, MD, Orthopedics and Traumatology Department, Modena Policlinic, University of Modena and Reggio Emilia, via del Pozzo 71, 41124 Modena, Italy. raffaele.mugnai@gmail.com
Telephone: +39-059-4223717
Fax: +39-059-4224313

Received: July 4, 2015

Peer-review started: July 12, 2015

First decision: September 30, 2015

Revised: November 14, 2015

Accepted: December 7, 2015

Article in press: December 8, 2015

Published online: February 18, 2016

Abstract

AIM: To review the current literature regarding corrective

osteotomies to provide the best evidence of the rule of bone grafting.

METHODS: Our MEDLINE literature search included 280 studies using the following key words "Malunited distal radius fracture" and 150 studies using key words "Corrective osteotomy of the distal radius". Inclusion criteria were: Malunited distal radial, extra articular fracture, volar locking plate, use of iliac bone graft (cancellous or corticocancellous), non-use of bone graft. Twelve studies met the inclusion criteria.

RESULTS: Seven of the 12 studies considered, described the use of a graft; the remaining five studies didn't use any graft. Type of malunion was dorsal in most of the studies. The healing time was comparable using the graft or not (mean 12.5 wk), ranging from 7.5 to 16 wk. The mean disabilities of the arm, shoulder and hand score improvement was 23 points both in the studies that used the graft and in those not using the graft.

CONCLUSION: This review demonstrated that corrective osteotomy of extra-articular malunited fractures of the distal radius treated by volar locking plate does not necessarily require bone graft.

Key words: Radial fracture; Osteotomy; Graft; Volar plate; Malunion

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The aim of this study was to review the current literature regarding corrective osteotomies in malunion of the distal radius to provide the best evidence of the rule of bone graft. The results of this review demonstrated that corrective osteotomy of extra-articular malunited fractures of the distal radius treated by volar locking plate does not necessarily require bone graft. Rate of union and functional outcomes were comparable.

Mugnai R, Tarallo L, Lancellotti E, Zambianchi F, Di Giovine E, Catani F, Adani R. Corrective osteotomies of the radius: Grafting or not? *World J Orthop* 2016; 7(2): 128-135 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/128.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.128>

INTRODUCTION

Distal radius fractures represent the 10%-12% of all fractures^[1-3]. One of the most common complication following distal radial fractures is malunion, especially when treated with close reduction and cast immobilization^[4]. Patients with symptomatic malunions of the distal radius usually present with wrist pain; restricted wrist range of motion (ROM), especially supination; reduced grip strength; unsightly appearance; late neuropathy especially of the median nerve, with compression at the carpal tunnel^[5-7]. Corrective osteotomy aims to restore anatomic configuration and improve function in unsatisfied patients.

Over the last few years, various corrective osteotomy techniques have been characterized^[1,6,8]. Although opening wedge osteotomy through a dorsal approach, using bone graft and non-locking plates has been in the past years the most widely recommended technique for treating distal radius malunion, this procedure requires an extensive dorsal approach and often determines extensor tendons irritation. Recently, with the introduction of fixed-angle plates, interest in performing these osteotomies through a volar approach has increased^[9,10]. According to the opening wedge treatment of a fracture united in a position of abnormality or deformity, a 3-D structural defect is produced by the surgeon in the distal radial metaphysis. The defect will then be filled with 3 different approaches: bone grafting, using a structural or non-structural autogenous corticocancellous bone graft; synthetic material [Norian, bone morphogenetic proteins (BMP), osteogenic protein-1 (OP-1)]; no bone graft^[11,12].

Bone graft

Corticocancellous bone can be derived from the iliac crest, distal femur, proximal tibia, fibula, distal radius and olecranon. Generally, the most used kind of bone graft is the autograft. Defects of a length smaller than 5 to 6 cm are well managed by nonvascularized iliac crest bone grafts, if in presence of well-perfused soft tissues and in absence of any active infection. Therefore they usually represent the first choice treatment of the defect created by the osteotomy. Bone graft helps to maintain the surgical corrections but with possible donor site morbidity: Persistent and chronic pain, serious discharge, nerve injury with meralgia, paresthesia, infection, fractures, pelvic instability, hematoma, cosmetic defects, hernia, ureteral injuries, arterial injuries^[12]. Moreover, sometimes it is not always feasible to shape a structural bone graft based on the dimensions of the defect

precisely^[13]. Studies have demonstrated that osteotomies filled with cancellous or corticocancellous grafts give comparable results^[14]. Anyway, cancellous is recognised to have three advantages over corticocancellous graft: first, it has no need for a specific anatomic configuration, since it can be totally compressed to stuff the defect, it gives the possibility to bypass the long procedure to prepare a structural graft, and lastly, it is not that difficult to applicate plate and screws (no displacement during the fixation) (Figures 1 and 2).

Synthetic graft

Autologous bone grafts can be replaced by bone substitute to elude donor site morbidity. Hydroxyapatite (HA) and calcium-sulphate (CS) are mineral-based substitutes for osteoconductive bone grafts. Osteotomies of malunited distal radial fractures^[15] and surgery of distal radial fractures^[16] has seen the use of HA as a substitute. Even tough the time lapse of resorbing graft is of years, it should have the strength necessary to absorb stress until the bone has formed. Although CS has been shown to be highly biocompatible, the resorption rate it is too rapid to be used in fracture treatment. Indeed the CS resorption is faster than the new bone formation; potentially causing hardware failure that can be avoided by maintaining a cortical contact across the osteotomy site^[16,17].

Osteoconductive bone graft substitutes

Extensive research has been conducted on osteoconductive alternatives, associated with growth factors and proteins such as BMPs. Mesenchymal stem cells have been seen to differentiate into chondrocytes and osteoblasts driven by the primitive induction of the BMPs, which are members of the transforming growth factor- β . Preclinical effectiveness investigation on BMPs took to subsequent clinical introduction of the most powerful BMPs, BMP-2 and BMP-7^[18,19]. OP-1, which also goes under the name of recombinant BMP-7, has been known for its osteoinductive properties. Animal and clinical trials showed therapeutic potential in more than a study. Demonstration of the efficacy of this grafts has been documented in spinal fusion, fibular defects, tibial non-union, and most recently also in pelvic girdle non-union^[19,20]. According to Ekrol *et al*^[20], OP-1 substitute has been shown not to elicit the same stability and stress absorption as bone graft across the osteotomy site; furthermore using the combination of a plate with OP-1 resulted in healing of the osteotomy but with a slower rate than autogenous bone graft.

No bone graft

Bone graft seems to be not always necessary when the distal malunion is extra articular and it's treated with a locking plate: The absence of bone graft seems not to adversely affect time to union and functional outcome.

In this case correction should be achieved in the coronal and sagittal planes by having the distal radius



Figure 1 Preoperative X-rays and 3D-computed tomography evaluation showing an extra-articular dorsal malunion in a 36 years old man.

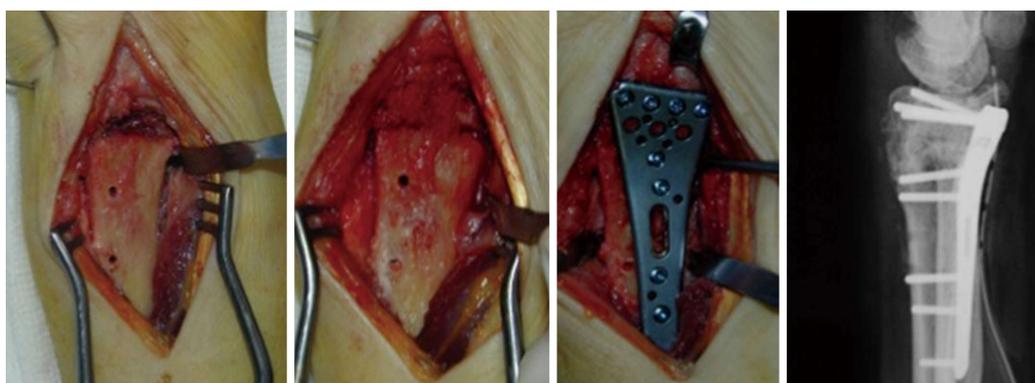


Figure 2 Intraoperative view and post-operative X-rays of the surgical procedure using a volar locking plate and cancellous bone graft.



Figure 3 Preoperative X-rays showing an extra-articular dorsal malunion in a 51 years old man.

conform to the tilt of the plate. It can be useful to maintain a volar cortical contact following corrective osteotomy, to ensure the physiological transmission of the force vector through the synthesis, from the distal to the proximal segment of the radius^[21] (Figures 3-5).

MATERIALS AND METHODS

Our MEDLINE literature search included 280 studies using the following key words "Malunited distal radius fracture" and 150 studies using key words "Corrective osteotomy of the distal radius". Inclusion criteria were: Malunited distal radial, extra articular fracture, volar locking plate, use of iliac bone graft (cancellous or corticocancellous), non use of bone graft. Twelve studies met the inclusion criteria. Although important, time of healing and clinical outcome, were not reported in all the studies included in the review.

RESULTS

For each study the number of evaluated patients, surgical technique (graft or not), number of patients enrolled, type of malunion, time of healing and functional recovery regarded as disabilities of the arm, shoulder and hand (DASH) score, pain improvement [visual analogue scale (VAS) and any eventual post-



Figure 4 Intraoperative X-rays showing corrective osteotomy of extra-articular dorsally displaced malunion of the distal radius treated by volar locking plate without bone graft, and maintaining volar cortical contact.

surgical complication (Table 1) were reported. In 7 out of the 12 studies included the graft was used: Iliac crest corticocancellous bone graft in 4 studies and iliac crest cancellous bone graft in 3. Moreover Malone *et al*^[22] used crushed cancellous allograft in 1 case and Wada *et al*^[23] tricalcium phosphate. In the remaining five studies grafting was not described. Despite this, the number of patients of all studies treated with graft was inferior to the number of those treated without graft (97 vs 104). Type of malunion was dorsal in most of the studies. The healing time was comparable using the graft or not (mean 12.5 wk), ranging from 7.5^[24] to 16^[25,26] wk. The mean DASH score improvement was 23 points both in the studies describing the use of the graft (range, 11-46)^[22-24,27-29], and in those not using the graft (range, 13-28)^[25,30-32]. Finally, few studies reported postoperative complications^[11,22,23,26,29,32]. Among the majority of the studies neither complications nor significant correction loss were indicated after surgery, even in elderly people. The results of the main evaluated literature are summarized in Table 1.

DISCUSSION

The majority of the examined literature used the bone graft to fix the remaining defect with corticocancellous or cancellous autogenous bone from the iliac crest. Gradl *et al*^[27] employed iliac crest corticocancellous bone graft in all case of malunion. He included in his study 18 patients treated using a palmar approach in 14



Figure 5 X-rays performed 3 mo post-operatively showing the healing process in progress.

cases and a combined approach (palmar + dorsal) in 4 cases. There were 7 palmar and 11 dorsal malunions, and remaining defects were fixed with corticocancellous autogenous bone graft from the iliac crest in 14 patients, and cancellous bone graft from the radius in one patient. At a mean 7 years of follow-up wrist ROM improved significantly in all cases and the DASH score decreased significantly from 59 to 23 points.

Treatment with transverse opening wedge osteotomy with oblique iliac bone graft of volarly malunited distal radius fractures led to a significant improvement in DASH score as reported by Sato *et al*^[24] in 2009. All patients were analyzed at a mean 25 mo of follow-up. Mean preoperative VAS scale was 45, improving significantly to 3 postoperatively. Range of wrist motion improved in all 28 patients, with supination range improving from 16° preoperatively to 80° postoperatively. Mean DASH score improvement from 55 to 9 postoperatively. X-rays evaluation showed an improvement of the volar tilt from 32° preoperatively to 10° postoperatively, and radial inclination increased from 17° to 21°. Preoperative ulnar variance of 5.9 mm was corrected to -0.1 mm postoperatively. Fifty-two days was the average time for bony union at osteotomy site (young patients, 51 d; older patients, 54 d).

Many authors described complications following the surgical treatment of dorsal malunion: Extensor tenosynovitis and, sometimes, tendon ruptures connected with the use of dorsal plates^[20,33,34]. Keller *et al*^[35] evaluated a series of 49 cases that underwent dorsal plating of the distal radius, reporting, at 32 mo follow-up, an average DASH score of 14.4 with good motion and grip strength. To be noted that 37 of the 49 patients required plate removal and of the 12 patients who did not undergo plate removal, one patient suffered a rupture of the extensor indicis proprius. It's common opinion among the authors that extensor tendon complications are the result of the profile of the dorsal plate^[21,27], but more recent studies claim that this complication can occur even with low-profile plates. Moreover screw placement is important: Gradl *et al*^[27] reported in one case the development of symptomatic tendinitis of the extensor pollicis longus tendon due to dorsal protrusion

Table 1 Results of the main evaluated literature

Ref.	No. of patients	Graft	Type of malunion	Time to healing	Clinical outcome (DASH)	Pain (VAS)	Complications
Gradl <i>et al</i> ^[27]	14	ICCCBG in all cases	Dorsal in 7 cases; volar in 4 cases	Not reported	36	4.2 ± 2.9	None
Malone <i>et al</i> ^[22]	3	ICCCBG in 2 cases; CCA in 1 case	Dorsal in all cases	9 wk	12	3.3	1 post-traumatic fracture
Peterson <i>et al</i> ^[28]	8	ICCCBG in all cases	Dorsal in 6 cases; volar in 2 cases	Not reported	10.8	Not reported	None
Rothenfluh <i>et al</i> ^[29]	14	ICCBG in all cases	Dorsal in all cases	12 wk	17.3	3.59	Secondary dislocation of the distal fragment was observed 21 d after surgery in 1 case
Wada <i>et al</i> ^[23]	16	ICCBG or tricalcium phosphate bone substitute	Dorsal and volar	13 wk	14	Significant improvement	2 delayed unions
Sato <i>et al</i> ^[24]	28	ICCCBG in all cases	Volar in all cases	7.5 wk	46	4.2	None
Miyake <i>et al</i> ^[26]	10	ICCBG in all cases	Dorsal in all cases	16 wk	Not reported	Significant improvement	Early postoperative screw loosening in 2 cases
Farshad <i>et al</i> ^[11]	28	None	Not specified	Not reported	Not reported	Not reported	Plate bending in 6 cases
Mahmoud <i>et al</i> ^[32]	22	None	Dorsal in all cases	10.4 wk	21.6 ± 13.5	3.4 ± 1.5	Intraoperative split in the shaft of the radius in 1 case CRPS in 1 case Residual pain in 2 cases
Opel <i>et al</i> ^[30]	20	None	Not specified	12 wk	13.4	Not reported	None
Ozer <i>et al</i> ^[31]	14	None	Dorsal in all cases	11 wk	28	Not reported	None
Tarallo <i>et al</i> ^[25]	20	None	Dorsal in all cases	16 wk	28.5	0.8	None

VAS: Visual analogue scale; DASH: Disabilities of the arm, shoulder and hand; ICCCBG: Iliac crest cortico cancellous bone graft; CCA: Crushed cancellous allograft; ICCBG: Iliac crest cancellous bone graft; CRPS: Complex regional pain syndrome.

of screw tips after corrective osteotomy with a palmar locking plate and autogenous bone grafting. Malone *et al*^[22] emphasized the role of the volar plate including structural bone grafting: Four corrective osteotomies has been performed using the volar approach for dorsally angulated malunion of distal radius fracture with a volar plate; two patients received autologous iliac crest bone graft, 1 patient received crushed cancellous allograft, and 1 patient had a distal ulna resection for ulnar impaction symptoms and the distal ulna was used as a source for the bone graft. The authors came to the concept that the stiff characteristics of fixed angle volar plates could provide an alternative to the traditional techniques of distal radius osteotomy including structural bone grafting and dorsal plate fixation or external fixation. Comparable results in terms of anatomic restoration of the distal radius, ROM improvement in the radiocarpal joint, and restoration of the anatomic relationships of the distal radioulnar joint were obtained by Rothenfluh *et al*^[29], Wada *et al*^[23], and Peterson *et al*^[28]. All these authors used bone graft from the iliac crest with a comparable DASH scores and no complications. Only Rothenfluh *et al*^[29] reported in one case a secondary dislocation of the distal fragment observed 21 d after volar osteotomy. In his study Rothenfluh *et al*^[29] compared the results of dorsal approach plus structural trapezoidal bone graft stabilized using a thin round-hole mini-fragment plate, with palmar approach plus nonstructural cancellous bone chips and a palmar fixed-angle plate, suggesting comparable results to those achieved with dorsal osteotomy and the interposition of cortico-cancellous bone graft. However, the palmar approach determined a

more favorable effect on wrist flexion, entailing lower complication rates, mainly represented by extensor tendonitis and hardware removal.

Several articles treated corrective osteotomy without bone graft and the first reports concerning this topic dates back to 1930s^[36]. In recent literature, Mahmoud *et al*^[32] described the results of 22 corrective osteotomies of extra-articular dorsally-angulated malunited fractures of the distal radius fixed by a volar locked plate without the use of bone graft. Radiological healing was achieved in all patients at a mean of 10.4 wk (8 to 14). At a mean of 18 (12 to 25) mo of follow-up the DASH score improved from 34.5 points to 12.9; improvements in the VAS score and grip strength were respectively 3.4 points and 17.4 kg; radiological correction of the deformity and ROM improvement were achieved in all cases. Complications occurred in six cases (27%): an intraoperative longitudinal split occurred in the shaft of the radius in one patient, requiring an interfragmentary compression screw; one patient suffered a transient median nerve neuritis; another patient suffered from CRPS, which was healed by physiotherapy; a prominent screw determined tendon impingement and required removal; residual pain on the ulnar side of the wrist due to ulnar impaction was encountered in two patients, requiring ulnar shortening. Tarallo *et al*^[25] treated 20 patients for symptomatic dorsally malunited extra-articular fractures of the distal radius with osteotomy and a volar locking plate without additional bone graft. The authors reported, at a mean 50 mo of follow-up, a significant improvement in pain level, ROM, grip strength, and DASH score.

An important factor to consider is that bone healing is determined by several factors, including cell differentiation, compromise of vascularity, and mechanical stability^[37]. Sheer *et al.*^[37], in a recent study, concluded that although there are few data on metaphyseal bone healing, there are some indications that it adheres to the same biomechanical principles as diaphyseal bone healing, with some differences concerning bone formation, which may follow different paths. The cortical contact between the osteotomy fragments represents an important factor, too. Ozer *et al.*^[31], investigated this aspect underlining the importance to maintain a volar cortical contact following the placement of the volar locking plate in order to obtain a better outcome, especially in extra-articular malunited fractures of the distal radius. They state that in such cases, it would not be necessarily required the use of bone graft.

The use of autogenous bone grafts has been reported to have high complication rates, with associated morbidity of up to 73%, and an additional operative time averaging 20 min^[31]. The most important complication reported by several authors is donor site morbidity, especially at the iliac crest. Minor complications, occurring in 7.1%-39% of patients, include persistent pain at the harvest site, sensory nerve injury, hematoma or seroma, and superficial infection^[38,39]. Concerning the use of a synthetic material, such products come with an inherent advantage of no donor site morbidity; however their use also come with a high cost of production and sometimes a potentially low, but real, risk of disease transmission. Abramo *et al.*^[18] evaluated 25 consecutive patients with a dorsal malunion after a distal radius fracture treated with corrective osteotomy using a dorsal approach. A TriMed buttress pin and a radial pin plate were used, and calcium phosphate mixture (Norian SRS) as bone substitute. At a 1-year follow-up grip strength increased from 62% of the contralateral hand to 82%, with a DASH score improvement of 12 points. Minor complications involving transient tingling and numbness from the radial nerve branches were reported initially in 6 cases, but disappeared by the last follow-up. One major complication occurred: The bone substitute fragmented before osseous union and the plate and screws broke 2 mo postoperatively. The patient was re-operated using conventional bone grafting and fixation with a dorsal AO plate.

Jepegnanam *et al.*^[40] reported on early mechanical failure of injectable calcium sulfate, leading to implant failure in 2 elderly patients who had corrective osteotomies for malunited distal radius fractures. Faster resorption might have specific advantages under certain conditions but might also be disadvantageous if it is required to contribute to mechanical support for many weeks or months. The authors hypothesized that the failures occurred because new bone formation did not occur rapidly enough to replace resorption of the grafted material.

Jepegnanam *et al.*^[40], suggest that graft substitutes with a faster resorption rate should be used with caution

in patients with expected slow bone healing. The major stability of bone graft compared with synthetic material is also emphasized by Ekrol *et al.*^[20]. They compared the OP-1 and autogenous graft for metaphyseal defects after osteotomy of the distal radius, concluding that OP-1 does not confer the same stability as bone graft, reducing the capacity for healing and resulting in osteolysis.

Conclusion

The results of this review demonstrate that corrective osteotomy of extra-articular malunited distal radius fractures treated by volar locking plate does not necessarily require the use of bone graft. Rate of union and functional outcomes are comparable to the use of bone graft. We suggest maintaining a volar cortical contact following corrective osteotomy, to ensure the physiological transmission of the force vector through the synthesis, from the distal segment of the radio to the proximal one.

Bone grafts however, remain a valuable support in this type of surgery, especially to fill gaps when a large defect is created. Synthetic materials come with an inherent advantage of no donor site morbidity but it seems that they do not confer the same stability as bone graft. Their use is limited by faster resorption rate than bone graft, so they should be used with caution in patients with expected slow bone healing rate.

COMMENTS

Background

Different techniques for corrective osteotomy have been described in recent years; although opening wedge osteotomy through a dorsal approach, using bone graft and non-locking plates has been in the past years the most widely recommended technique for treating distal radius malunion, this procedure requires an extensive dorsal approach and often determines extensor tendons irritation. Recently, with the introduction of fixed-angle plates, interest in performing these osteotomies through a volar approach has increased.

Research frontiers

According to the opening wedge treatment of a malunited fracture, the surgeon creates a 3-dimensional structural defect in the distal radial metaphysis, which will be filled with 3 different approaches: Bone grafting, using a structural or non-structural autogenous corticocancellous bone graft; synthetic material (Norian, bone morphogenic proteins, osteogenic protein-1); no bone graft.

Innovations and breakthroughs

Current publication is the first systematic review, which summarize published data concerning the use of bone graft in corrective osteotomy of extra-articular malunited fractures of the distal radius treated by volar locking plate. The results of this review demonstrate that corrective osteotomy of extra-articular malunited fractures of the distal radius treated by volar locking plate does not necessarily require the use of bone graft. Rate of union and functional outcomes are comparable to the use of bone graft. However bone graft still represents a valuable solution in this type of surgery, especially to fill the gap when a large osteotomy is performed.

Applications

Given similar rates of union, functional outcomes and complications occurrence, the authors suggest that when a volar cortical contact is maintained following corrective osteotomy the use of bone graft is not necessarily required.

Terminology

Cancellous bone is the meshwork of spongy tissue (trabeculae) of mature adult bone. The most common harvesting site for autogenous cancellous bone graft is the iliac crest, tibial crest, humeral greater tubercle and greater trochanter of femur. Cancellous bone autograft offers the considerable amounts of viable cells that boost the osteogenesis, matrix protein that promotes the osteoinduction and bone matrix that encourage the osteoinduction. Cancellous bone grafts lack biomechanical strength and do not supply structural support. Corticocancellous grafts yield significant mechanical strength and can be used to either replace bone losses or to augment the mechanical stability of the fixation. The most common sites for harvesting corticocancellous bone autograft are ribs, the anterosuperior iliac crest and the posterior iliac crest.

Peer-review

This is a good study.

REFERENCES

- 1 **Slagel BE**, Luenam S, Pichora DR. Management of post-traumatic malunion of fractures of the distal radius. *Orthop Clin North Am* 2007; **38**: 203-216, vi [PMID: 17560403]
- 2 **Lidstrom A**. Fractures of the distal end of the radius. A clinical and statistical study of end results. *Acta Orthop Scand Suppl* 1959; **41**: 1-118 [PMID: 14416798]
- 3 **Bacorn RW**, Kurtzke JF. Colles' fracture; a study of two thousand cases from the New York State Workmen's Compensation Board. *J Bone Joint Surg Am* 1953; **35-A**: 643-658 [PMID: 13069552]
- 4 **Amadio PC**, Botte MJ. Treatment of malunion of the distal radius. *Hand Clin* 1987; **3**: 541-561 [PMID: 3320065]
- 5 **Sharpe F**, Stevanovic M. Extra-articular distal radial fracture malunion. *Hand Clin* 2005; **21**: 469-487 [PMID: 16039458]
- 6 **Jupiter JB**, Fernandez DL. Complications following distal radial fractures. *Instr Course Lect* 2002; **51**: 203-219 [PMID: 12064104]
- 7 **Schmitz MA**, Finnegan M, Natarajan R, Champine J. Effect of smoking on tibial shaft fracture healing. *Clin Orthop Relat Res* 1999; (**365**): 184-200 [PMID: 10627703]
- 8 **Sennwald G**, Fischer M. [Correction of distal radial malunion by forward-sliding osteotomy. 3 case reports]. *Ann Chir Main Memb Supr* 1993; **12**: 124-129 [PMID: 7688234]
- 9 **Watson HK**, Castle TH. Trapezoidal osteotomy of the distal radius for unacceptable articular angulation after Colles' fracture. *J Hand Surg Am* 1988; **13**: 837-843 [PMID: 3271005]
- 10 **Posner MA**, Ambrose L. Malunited Colles' fractures: correction with a biplanar closing wedge osteotomy. *J Hand Surg Am* 1991; **16**: 1017-1026 [PMID: 1748745]
- 11 **Farshad M**, Hess F, Nagy L, Schweizer A. Corrective osteotomy of distal radial deformities: a new method of guided locking fixed screw positioning. *J Hand Surg Eur Vol* 2013; **38**: 29-34 [PMID: 22184783 DOI: 10.1177/1753193411433227]
- 12 **Läftman P**, Sigurdsson F, Strömberg L. Recovery of diaphyseal bone strength after rigid internal plate fixation. An experimental study in the rabbit. *Acta Orthop Scand* 1980; **51**: 215-222 [PMID: 7435177]
- 13 **Younger EM**, Chapman MW. Morbidity at bone graft donor sites. *J Orthop Trauma* 1989; **3**: 192-195 [PMID: 2809818]
- 14 **Conway JD**. Autograft and nonunions: morbidity with intramedullary bone graft versus iliac crest bone graft. *Orthop Clin North Am* 2010; **41**: 75-84; table of contents [PMID: 19931055 DOI: 10.1016/j.ocl.2009.07.006]
- 15 **Luchetti R**. Corrective osteotomy of malunited distal radius fractures using carbonated hydroxyapatite as an alternative to autogenous bone grafting. *J Hand Surg Am* 2004; **29**: 825-834 [PMID: 15465231]
- 16 **Ring D**, Roberge C, Morgan T, Jupiter JB. Osteotomy for malunited fractures of the distal radius: a comparison of structural and nonstructural autogenous bone grafts. *J Hand Surg Am* 2002; **27**: 216-222 [PMID: 11901380]
- 17 **Peltier LF**. The use of plaster of Paris to fill defects in bone. *Clin Orthop* 1961; **21**: 1-31 [PMID: 14485018]
- 18 **Abramo A**, Tagil M, Geijer M, Kopylov P. Osteotomy of dorsally displaced malunited fractures of the distal radius: no loss of radiographic correction during healing with a minimally invasive fixation technique and an injectable bone substitute. *Acta Orthop* 2008; **79**: 262-268 [PMID: 18484254 DOI: 10.1080/17453670710015085]
- 19 **Giannoudis PV**, Tzioupis C. Clinical applications of BMP-7: the UK perspective. *Injury* 2005; **36** Suppl 3: S47-S50 [PMID: 16188550]
- 20 **Ekrol I**, Hajducka C, Court-Brown C, McQueen MM. A comparison of RhBMP-7 (OP-1) and autogenous graft for metaphyseal defects after osteotomy of the distal radius. *Injury* 2008; **39** Suppl 2: S73-S82 [PMID: 18804577 DOI: 10.1016/S0020-1383(08)70018-4]
- 21 **Lozano-Calderón S**, Moore M, Liebman M, Jupiter JB. Distal radius osteotomy in the elderly patient using angular stable implants and Norian bone cement. *J Hand Surg Am* 2007; **32**: 976-983 [PMID: 17826549]
- 22 **Malone KJ**, Magnell TD, Freeman DC, Boyer MI, Placzek JD. Surgical correction of dorsally angulated distal radius malunions with fixed angle volar plating: a case series. *J Hand Surg Am* 2006; **31**: 366-372 [PMID: 16516729]
- 23 **Wada T**, Tatebe M, Ozasa Y, Sato O, Sonoda T, Hirata H, Yamashita T. Clinical outcomes of corrective osteotomy for distal radial malunion: a review of opening and closing-wedge techniques. *J Bone Joint Surg Am* 2011; **93**: 1619-1626 [PMID: 21915577 DOI: 10.2106/JBJS.J.00500]
- 24 **Sato K**, Nakamura T, Iwamoto T, Toyama Y, Ikegami H, Takayama S. Corrective osteotomy for volarly malunited distal radius fracture. *J Hand Surg Am* 2009; **34**: 27-33, 33.e1 [PMID: 19121727 DOI: 10.1016/j.jhsa.2008.09.018]
- 25 **Tarallo L**, Mugnai R, Adani R, Catani F. Malunited extra-articular distal radius fractures: corrective osteotomies using volar locking plate. *J Orthop Traumatol* 2014; **15**: 285-290 [PMID: 25017024 DOI: 10.1007/s10195-014-0307-x]
- 26 **Miyake J**, Murase T, Moritomo H, Sugamoto K, Yoshikawa H. Distal radius osteotomy with volar locking plates based on computer simulation. *Clin Orthop Relat Res* 2011; **469**: 1766-1773 [PMID: 21203873 DOI: 10.1007/s11999-010-1748-z]
- 27 **Gradi G**, Jupiter J, Pillukat T, Knobe M, Prommersberger KJ. Corrective osteotomy of the distal radius following failed internal fixation. *Arch Orthop Trauma Surg* 2013; **133**: 1173-1179 [PMID: 23708289 DOI: 10.1007/s00402-013-1779-5]
- 28 **Peterson B**, Gajendran V, Szabo RM. Corrective osteotomy for deformity of the distal radius using a volar locking plate. *Hand (N Y)* 2008; **3**: 61-68 [PMID: 18780123 DOI: 10.1007/s11552-007-9066-y]
- 29 **Rothenfluh E**, Schweizer A, Nagy L. Opening wedge osteotomy for distal radius malunion: dorsal or palmar approach? *J Wrist Surg* 2013; **2**: 49-54 [PMID: 24436789 DOI: 10.1055/s-0032-1326725]
- 30 **Opel S**, Konan S, Sorene E. Corrective distal radius osteotomy following fracture malunion using a fixed-angle volar locking plate. *J Hand Surg Eur Vol* 2014; **39**: 431-435 [PMID: 24051477 DOI: 10.1177/1753193413497636]
- 31 **Ozer K**, Kiliç A, Sabel A, Ipaktchi K. The role of bone allografts in the treatment of angular malunions of the distal radius. *J Hand Surg Am* 2011; **36**: 1804-1809 [PMID: 22036280 DOI: 10.1016/j.jhsa.2011.08.011]
- 32 **Mahmoud M**, El Shafie S, Kamal M. Correction of dorsally-malunited extra-articular distal radius fractures using volar locked plates without bone grafting. *J Bone Joint Surg Br* 2012; **94**: 1090-1096 [PMID: 22844051 DOI: 10.1302/0301-620X.94B8.28646]
- 33 **Schnur DP**, Chang B. Extensor tendon rupture after internal fixation of a distal radius fracture using a dorsally placed AO/ASIF titanium pi plate. Arbeitsgemeinschaft für Osteosynthesefragen/ Association for the Study of Internal Fixation. *Ann Plast Surg* 2000; **44**: 564-566 [PMID: 10805309]
- 34 **Simic PM**, Robison J, Gardner MJ, Gelberman RH, Weiland AJ, Boyer MI. Treatment of distal radius fractures with a low-profile dorsal plating system: an outcomes assessment. *J Hand Surg Am*

- 2006; **31**: 382-386 [PMID: 16516731]
- 35 **Keller M**, Steiger R. [Open reduction and internal fixation of distal radius extension fractures in women over 60 years of age with the dorsal radius plate (pi-plate)]. *Handchir Mikrochir Plast Chir* 2006; **38**: 82-89 [PMID: 16680663]
- 36 **Meyerdig HW**, Overton LM. Malunited fracture of the lower end of the radius (Colles' fracture) treated by osteotomy. *Minnesota Medicine* 1935; **18**: 84-89
- 37 **Scheer JH**, Adolfsson LE. Non-union in 3 of 15 osteotomies of the distal radius without bone graft. *Acta Orthop* 2015; **86**: 316-320 [PMID: 25619425 DOI: 10.3109/17453674.2015.1007415]
- 38 **Westrich GH**, Geller DS, O'Malley MJ, Deland JT, Helfet DL. Anterior iliac crest bone graft harvesting using the corticocancellous reamer system. *J Orthop Trauma* 2001; **15**: 500-506 [PMID: 11602833]
- 39 **Dimitriou R**, Mataliotakis GI, Angoules AG, Kanakaris NK, Giannoudis PV. Complications following autologous bone graft harvesting from the iliac crest and using the RIA: a systematic review. *Injury* 2011; **42** Suppl 2: S3-15 [PMID: 21704997 DOI: 10.1016/j.injury.2011.06.015]
- 40 **Jepegnanam TS**, von Schroeder HP. Rapid resorption of calcium sulfate and hardware failure following corrective radius osteotomy: 2 case reports. *J Hand Surg Am* 2012; **37**: 477-480 [PMID: 22305728 DOI: 10.1016/j.jhsa.2011.12.020]

P- Reviewer: Anand A, Ertem K **S- Editor:** Ji FF

L- Editor: A **E- Editor:** Liu SQ



Photogrammetry as a tool for the postural evaluation of the spine: A systematic review

Tássia Silveira Furlanetto, Juliana Adami Sedrez, Cláudia Tarragô Candotti, Jefferson Fagundes Loss

Tássia Silveira Furlanetto, Juliana Adami Sedrez, Cláudia Tarragô Candotti, Jefferson Fagundes Loss, Exercise Research Laboratory, Federal University of Rio Grande do Sul, Porto Alegre 90690-200, Brazil

Author contributions: Furlanetto TS and Sedrez JA gathered, analyzed and interpreted the data and drafted the manuscript; Candotti CT and Loss JF Study conceived and designed the study and performed the critical review.

Conflict-of-interest statement: All the authors declare that they have no competing interests.

Data sharing statement: The dataset is available from the corresponding author at jefferson.loss@ufrgs.br.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Jefferson Fagundes Loss, PHD, Exercise Research Laboratory, Federal University of Rio Grande do Sul, Rua Felizardo, 750, Porto Alegre 90690-200, Brazil. jefferson.loss@ufrgs.br
Telephone: +55-51-33085822

Received: May 4, 2015

Peer-review started: May 5, 2015

First decision: June 20, 2015

Revised: July 24, 2015

Accepted: December 3, 2015

Article in press: December 4, 2015

Published online: February 18, 2016

Abstract

AIM: To evaluate the use of photogrammetry and

identify the mathematical procedures applied when evaluating spinal posture.

METHODS: A systematic search using keywords was conducted in the PubMed, EMBASE, Scopus, Science and Medicine® databases. The following inclusion criteria adopted were: (1) the use of photogrammetry as a method to evaluate spinal posture; (2) evaluations of spinal curvature in the sagittal and/or frontal plane; (3) studies published within the last three decades; and (4) written entirely in English. The exclusion criteria were: (1) studies which objective involved the verification of some aspect of validation of instruments; (2) studies published as abstracts and those published in scientific events; and (3) studies using evaluation of the anteriorization of the head to determine the angular positioning of the cervical spine. The articles in this review were included and evaluated for their methodological quality, based on the Downs and Black scale, by two independent reviewers.

RESULTS: Initially, 1758 articles were found, 76 of which were included upon reading the full texts and 29 were included in accordance with the predetermined criteria. In addition, after analyzing the references in those articles, a further six articles were selected, so that 35 articles were included in this review. This systematic review revealed that the photogrammetry has been using in observational studies. Furthermore, it was also found that, although the data collection methodologies are similar across the studies, in relation to aspects of data analysis, the methodologies are very different, especially regarding the mathematical routines employed to support different postural evaluation software.

CONCLUSION: With photogrammetry, the aim of the assessment, whether it is for clinical, research or collective health purposes, must be considered when choosing which protocol to use to evaluate spinal posture.

Key words: Lordosis; Kyphosis; Spine; Photogrammetry; Scoliosis; Posture

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: With photogrammetry, various spinal posture assessment protocols can be adopted. However, the literature lacks evidence to support the use of photogrammetry in accompanying postural treatment, whether for clinical or research purposes. When using photogrammetry in scientific research, a protocol or software that provides detailed postural analysis should be the first choice. In the clinical environment, the choice of protocol will depend on the objectives established for the patient by the physiotherapist. When dealing with a collective health situation, such as groups of schoolchildren, it is necessary to prioritize simpler protocols.

Furlanetto TS, Sedrez JA, Candotti CT, Loss JF. Photogrammetry as a tool for the postural evaluation of the spine: A systematic review. *World J Orthop* 2016; 7(2): 136-148 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i2/136.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i2.136>

INTRODUCTION

Photogrammetry is a widely used non-invasive technique for postural evaluation. It is a viable option for healthcare professionals and researchers in the field of posture^[1], possibly because it allows a succinct and accurate quantitative evaluation by recording subtle changes in posture in general^[2,3]. From the point of view of spinal evaluation, it is capable of providing information in the frontal and sagittal planes^[4,5]. Furthermore, the use of photogrammetry undoubtedly contributes to reducing exposure to radiation and thus enables the monitoring of postural treatment. However, the application of this technique in postural evaluation is directly dependent on both the collection procedures and the mathematical methods used to provide measurements and postural diagnoses, and which should provide all the necessary aspects of validation^[6,7].

Specifically regarding the application of photogrammetry in spinal evaluation, many studies have performed procedures to validate the technique^[4,6,8-11]. Furthermore, in clinical practice, photogrammetry can be useful for evaluating and monitoring changes in spinal treatments by comparing quantitative data on posture^[6,12]. Moreover, in scientific studies, its use may be helpful in both transverse and longitudinal observations and in intervention studies.

Although, according to the literature, the use of photogrammetry in spinal evaluation is widespread, its real applicability may be questioned, as it remains unclear how this technique is being used to monitor postural treatment or to map attitudes among populations in observational studies. Furthermore, many studies that have adopted the use of photogrammetry do not explain the methods used to generate the results

obtained, thus constituting veritable "black boxes", which makes it difficult for users both in clinical practice and in scientific research to apply this evaluation method. Hence, the objective of this systematic review was to evaluate the use of photogrammetry and to identify the mathematical procedures involved when it is applied to assess spinal posture.

MATERIALS AND METHODS

This study was a systematic review, in which the eligibility criteria were observational studies and randomized and nonrandomized clinical trials that have used photogrammetry as a tool to evaluate the spine in an attempt to understand its importance in the assessment of posture. The systematic review follows methods recommended by the Cochrane Collaboration^[13].

A systematic literature search was performed in the PubMed, Embase, Scopus, Science and MEDICINE® databases in the months of December 2013 and January 2014. The keywords used were found in the Health Sciences Descriptors (DeCS, Descritores em Ciências da Saúde), Medical Subject Headings or Emtree: ("Photogrammetry" OR "Digital Analysis" OR "Digital Photographs" OR "Digital photography") AND ("Spinal postural evaluation" OR "Spine" OR "Vertebral Column" OR "Column, Vertebral" OR "Columns, Vertebral" OR "Vertebral Columns" OR "Spinal Column" OR "Column, Spinal" OR "Columns, Spinal" OR "Spinal Columns" OR "Vertebra" OR "Vertebrae" OR "Lordosis" OR "Kyphosis" OR "Kyphoses" OR "Scoliosis" OR "Scolioses" OR "Posture" OR "Postures" OR "Spine Curvatures" OR "lumbar curvatures" OR "thoracic curvatures" OR "thoracic curve" OR "lordosis curve" OR "thoracic kyphosis" OR "lumbar lordosis"). The search was limited to articles written entirely in English, because it is the international language.

To constitute this systematic review, the articles identified by the initial search strategy had to meet the following inclusion criteria: (1) use photogrammetry as a method of postural evaluation; (2) evaluate the curvatures of the spine in the sagittal or frontal plane; (3) been published within the last three decades; and (4) been written entirely in English. The exclusion criteria were: (1) studies in which the objective involved verifying some aspect of instrument validation; (2) studies published as abstracts and published in scientific events; and (3) studies that used the evaluation of anteriorization of the head to determine the angular positioning of the cervical spine. These variables are believed to analyze different aspects of body posture and cannot be analyzed together.

All the search procedures, selection, quality assessment, data extraction and the reading of the articles were performed independently and individually by two reviewers. In case of any difference of opinion between the reviewers, a third reviewer was asked to appraise the article.

Initially, the studies were selected by reading the

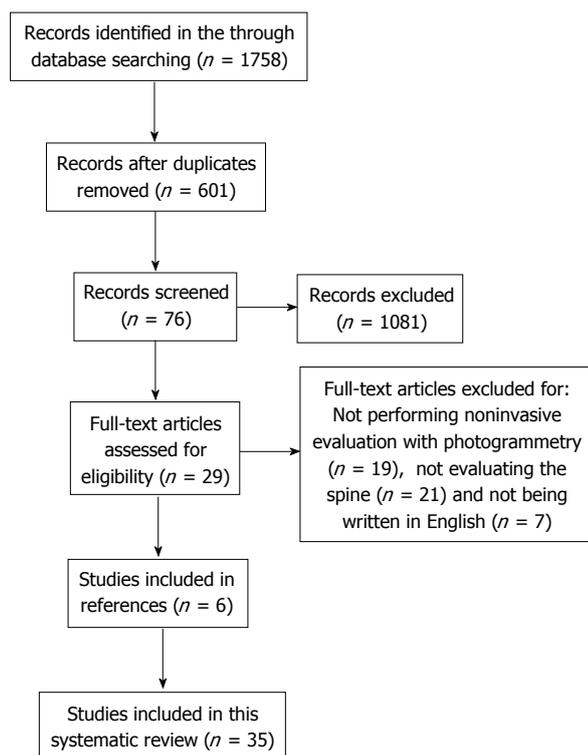


Figure 1 Flowchart of article selection.

titles and abstracts, and those considered to have the potential to be included in the search were read and analyzed in full. In those cases where the title and the abstract were inconclusive, the full article was obtained and read in order not to risk of leaving out important studies in this review. Complementing this process, the references of each included article were also checked in order to identify items not found in the electronic search.

The studies that met the inclusion criteria were evaluated for their methodological quality using the Downs and Black scale, which consists of a checklist of 26 criteria that are answered “yes”, “no” or “impossible to determine”^[14]. This scale was chosen because it is used to evaluate both observational studies and randomized clinical trials (RCTs), while some criteria are designed to assess RCTs exclusively, which were unnecessary in this systematic review. According to the guidelines for the use of the scale^[14], the assessment criteria can be chosen based on the study objective, thus in the present study those criteria referring solely to the assessment of RCTs were excluded, and only 12 criteria from the Downs and Black scale were used when assessing methodological aspects.

The Downs and Black scale does not define a minimum score when determining the quality of studies^[14]. Therefore, studies were not excluded based on their quality rating and only the total number of criteria rated as “yes” for each article was used. The higher the score for the criteria of article, the better methodological quality^[14].

RESULTS

Initially, 1758 articles were found from the keywords used. Of these, 601 were excluded because they were duplicates and 1081 did not meet the inclusion criteria. Thus, 76 studies were initially included in this systematic review. After reading the articles in full, 29 studies were found to meet all the inclusion criteria. Subsequently, their reference lists were analyzed and, based on this analysis, a further that 6 articles were found to meet the inclusion criteria, thus 35 articles were selected for inclusion in this systematic review (Figure 1).

Table 1 presents the assessment of the methodological quality based on Downs and Black scale of the studies selected for review. All 35 items had checklist scores higher or equal to 6. In addition, 9 studies had scores between 7 and 8; 19 studies had scores between 9 and 10; and 6 studies had scores between 11 and 12 (Table 1).

The 35 studies included in this review that use photogrammetry as a tool to evaluate the spine in the sagittal and frontal planes are presented and described (Table 2). The aspects related to the objective, the type of study, the methodology and the results of the studies are also shown.

Of the studies in which photogrammetry is used as a postural assessment tool, only one involves a randomized clinical trial, while the others are observational studies. Regarding study populations, most studies involved adults, followed by children and adolescents, while a few studies involved populations with specific diseases that may affect some aspect of posture was evaluated (Table 2).

The vast majority of studies included in this systematic review are concerned with evaluating the sagittal curvature of the spine, while scoliosis is evaluated in only eight studies. To achieve their objectives, several mathematical routines are used in the postural evaluation software programs to measure the alterations in the spine. Most, whether for the frontal or sagittal plane, used angular and/or linear values to measure the magnitude of the spinal alterations (Table 2).

DISCUSSION

This systematic review aimed to verify the applicability of photogrammetry and to identify the mathematical procedures involved in the use of this technique to evaluate the posture of the spine. Among the 35 articles included in this study, there is considerable similarity regarding the applicability of photogrammetry within scientific circles. However, there are important differences in the mathematical procedures used to evaluate the spine. Next, the articles included in this review were analyzed by groups, regarding the methodology used to collect and analyze data with photogrammetry: (1) type of study; (2) evaluated population; (3) region of the spine and type of alteration evaluated; and (4) types of

Table 1 Results of the quality assessment of studies by downs and black scale

Ref.	Criteria checklist downs and black												Total (No. of √)
	1	2	3	6	7	9	10	11	12	16	18	20	
Almeida <i>et al</i> ^[15]	√	X	√	X	√	√	√	?	?	√	√	√	8
Cheng <i>et al</i> ^[16]	√	√	√	√	√	√	√	?	?	√	√	√	10
Fortin <i>et al</i> ^[17]	√	√	√	√	√	√	√	?	?	√	√	√	10
Annetts <i>et al</i> ^[18]	√	√	√	√	√	√	√	X	X	√	√	√	10
Weber <i>et al</i> ^[19]	√	√	√	√	X	?	√	X	X	√	√	√	8
Edmondston <i>et al</i> ^[20]	√	√	√	√	√	√	√	X	X	√	√	√	10
Milanesi <i>et al</i> ^[21]	√	√	√	√	√	√	√	?	?	√	√	√	10
de Oliveira Pezzan <i>et al</i> ^[22]	√	√	√	√	√	√	√	?	?	√	√	√	10
Yang <i>et al</i> ^[23]	√	√	√	√	?	√	√	?	?	√	√	√	9
Silveira <i>et al</i> ^[24]	√	√	√	√	√	√	√	?	?	√	√	√	10
Iunes <i>et al</i> ^[25]	√	√	√	√	X	√	√	?	?	√	√	√	9
Belli <i>et al</i> ^[26]	√	√	√	√	√	√	X	√	√	√	√	√	11
Chase <i>et al</i> ^[27]	√	√	√	√	√	?	√	√	√	√	√	?	10
Iunes <i>et al</i> ^[12]	√	√	√	√	√	√	√	X	X	√	√	√	10
Iunes <i>et al</i> ^[28]	√	√	√	√	√	√	√	?	?	√	√	√	10
Penha <i>et al</i> ^[29]	√	√	√	√	√	√	√	√	√	√	√	√	12
Rodrigues <i>et al</i> ^[30]	√	√	√	√	√	√	√	X	X	√	√	√	10
Straker <i>et al</i> ^[31]	√	√	√	√	√	√	√	√	√	√	√	√	12
Iunes <i>et al</i> ^[32]	√	√	√	√	X	√	√	X	X	√	√	√	9
Smith <i>et al</i> ^[33]	√	√	X	√	√	√	√	?	?	√	√	√	9
Yi <i>et al</i> ^[33]	√	√	√	√	√	√	√	?	?	√	√	√	10
Min <i>et al</i> ^[34]	X	√	√	√	√	√	?	?	?	√	?	√	7
Straker <i>et al</i> ^[35]	√	√	√	√	√	√	√	√	√	√	√	?	11
Szopa <i>et al</i> ^[36]	√	√	√	√	√	X	√	?	?	√	?	√	8
Amsters <i>et al</i> ^[37]	√	√	√	√	√	√	X	?	?	√	?	X	7
O'Sullivan <i>et al</i> ^[38]	√	√	√	√	√	√	√	?	?	√	√	√	10
Milosavljevic <i>et al</i> ^[39]	√	√	√	√	√	√	√	√	√	√	√	√	12
Munhoz <i>et al</i> ^[40]	√	√	√	√	√	√	√	√	√	√	√	√	12
Lima <i>et al</i> ^[41]	√	√	√	√	X	?	√	?	?	√	√	?	7
Raine <i>et al</i> ^[42]	√	√	√	X	√	X	√	X	X	√	√	√	8
Christie <i>et al</i> ^[43]	√	√	√	√	√	√	√	?	?	√	√	√	10
Watson <i>et al</i> ^[44]	√	?	√	X	√	√	X	?	?	√	√	√	7
Raine <i>et al</i> ^[45]	√	√	√	√	√	√	√	X	X	√	√	√	10
Mitchell <i>et al</i> ^[46]	X	√	√	√	√	√	?	?	?	√	?	X	6
Dieck <i>et al</i> ^[47]	√	√	√	√	X	?	?	?	?	√	√	√	8

Downs and black criteria: (1) Is the hypothesis/objective clearly described? (2) Are the main results to be measured clearly described in the Introduction or Materials and Methods? (3) Were the characteristics of the patients included clearly described? (6) Are the main findings of the study clearly described? (7) Does the study estimate the random variability in the data of the main results? (9) Were the characteristics of the lost patients described in the study? (10) Were the true probability values reported for the main results? (11) Are the subjects asked to participate in the study representative of the entire population where they were recruited? (12) Are the subjects recruited to participate in the study representative of the entire population where they were recruited? (16) If any of the results of the study were based on "data dredging", was it clear? (18) Were statistical tests used to assess the main results appropriate? (20) Were the main results evaluated accurate (valid and reliable)? Responses to the criteria: √: Yes; X: No; ?: Unable to determine.

mathematical procedures.

Comparing the studies in which photogrammetry is used as a postural evaluation tool, only one study is a randomized clinical trial^[25], all the others being observational studies. The reason for not using this tool in "trial" studies of type "trials" is unclear, since photogrammetry is recognized as a valid and reproducible instrument for monitoring treatment progression, both in clinical practice and research^[5,6,25,48]. Among the possible explanations for these findings are the lack of free access software for evaluating the spine and/or recent use of digital photographs and analysis software for the use in large intervention studies^[1].

Furthermore, the difficulty involved in treating conditions related to spinal posture may also go some way to explain these results, since this body segment is highly influenced by mechanical, social, political and psychological factors^[49].

As nearly all the studies presented in this systematic review were cross-sectional, their objectives varied according to the population assessed, making it possible to evaluate some specific characteristics of spinal posture in the groups involved. Moreover, photogrammetry is particularly useful for that purpose because it is capable of recording subtle transformations and so is able to quantify the morphological variables related to posture^[2,3]. Some specific populations were evaluated using photogrammetry, such as adults^[12,19,20,42,45,47], children and teenagers^[3,29,31,35], pregnant women^[46] and athletes^[44]. In some studies, where the samples consisted of adults, some utensils (e.g., chairs and high-heeled shoes) are used in order to verify any change in the posture of the spine during their use^[18,22,32].

Similarly, some studies include patients with various diseases, where the authors believe they have a relationship with spinal posture. There are articles in which

Table 2 Synthesis of the 35 studies included in this systematic review

Ref.	Objective	Type of study	Methodology	Results
Almeida <i>et al</i> ^[15]	To assess the correlation between pulmonary function and posture; to investigate the correlation between body composition and body posture	Observational	<i>n</i> = 34 adult patients with asthma. Measurements: Bioelectrical impedance, spirometry, whole-body plethysmography, measurement of diffusing capacity for carbon monoxide and assessment of respiratory muscle strength. The lumbar lordosis was assessed by the pelvic anteversion (PAS)	The patients exhibit lumbar hyperlordosis. These postural abnormalities correlate with patients' pulmonary function and body composition
Cheng <i>et al</i> ^[16]	To investigate the influence of lower body stabilization and pencil design on body biomechanics (postural alterations) in children with CP	Observational	<i>n</i> = 14 children with CP. In the posterior view was measured the trunk lateral inclination angle and posterior superior iliac spine-C7/L4 angle; and in the lateral view was measured the trunk forward inclination angle (AutoCAD software)	A chair which provides proper positioning was effective in improving trunk posture in children with CP during handwriting activity. A pencil with assigned grip height or with a biaxial design, when compared with a regular one, could improve trunk alignment
Fortin <i>et al</i> ^[17]	To explore differences in standing and sitting postures and to compare differences between thoracic and thoraco-lumbar or lumbar scoliosis	Observational	<i>n</i> = 50 (29 thoracic scoliosis, 14 thoraco-lumbar scoliosis and 7 lumbar scoliosis). The cervical lordosis (sagittal plane) and scoliosis (frontal plane) was assessed by angles in standing and sitting positions (software program developed by their multidisciplinary team)	The cervical lordosis was not different in the two postures and scoliosis angle was significantly lower in the standing position. No significant difference was found for the index scoliosis angle in groups of scoliosis
Annetts <i>et al</i> ^[18]	To investigate the difference in lumbar angle and neck angle when comparing four seating designs; and consider the postures adopted on the four chairs in relation to an "ideal" posture	Observational	<i>n</i> = 14. The lumbar and neck angle was assessed in sit posture in the four seating designs (Matlab programme)	All chairs also resulted in a negative value for the lumbar region indicating a lordotic posture was adopted. All chairs resulted in a positive value for neck angle demonstrating the extent of the forward head position. No chair seemed to consistently produce an ideal posture across all regions
Weber <i>et al</i> ^[19]	To evaluate the relationship between cervical lordosis, and forward head posture and head position	Observational	<i>n</i> = 80 women. The cervical curvature was measured by the horizontal distance from a vertical line tangent (postural assessment software - SAPO®). Three angles measured the position of the head: Head flexion/extension (between C7, tragus and palpebral commissure), forward head posture A1 (between line of the tragus-C7 with the horizontal), and forward head posture A2 (between the external acoustic meatus, chin and sternal notch)	There were negative moderate and significant correlation between cervical lordosis and forward head posture A1. There were moderate and significant correlation between cervical lordosis and head flexion/extension
Edmondston <i>et al</i> ^[20]	To examine the extension mobility of the thoracic spine; and to evaluate the influence of the thoracic kyphosis on the thoracic extension range of motion, and the end range extension position	Observational	<i>n</i> = 40. The thoracic mobility was measured by kyphosis angle between T1, T6 e T12, in standing, sitting, 4-point kneeling, and prone lying (ImageJ Software)	The total sagittal range of motion in standing was 20.2° ± 6.6°, consisting of 8.7° ± 5.8° of extension and 11.5° ± 3.7° of flexion. The mean amount of thoracic angle was 21.6° ± 5.6°. The magnitude of the thoracic kyphosis was associated with the end range extension position but not with the range of motion toward extension
Milanesi <i>et al</i> ^[21]	To verify the impact of the mouth breathing occurred in the childhood on the body posture in the adult age	Observational	<i>n</i> = 24 study group (subjects with history of mouth breathing during childhood) and 20 control group. The cervical and lumbar lordosis were assessed by angles and distances; and the thoracic kyphosis was assessed by angle (postural evaluation software-SAPO v 0.68®)	The cervical lordosis angle and the cervical distance measures were larger in the study group. The lumbar lordosis angle was smaller in the study group, meaning greater lumbar lordosis in these subjects. No significant difference was observed between the groups for thoracic kyphosis and lumbar distance

de Oliveira Pezzan <i>et al</i> ^[22]	To analyze the influences of wearing wedge high-heeled shoes on lumbar lordosis angle among adolescents who were users and nonusers of high-heeled shoes and to correlate these angles with ages and the time of high-heel use	Observational	<i>n</i> = 50 UG and <i>n</i> = 50 NUG of high-heeled shoes. The photographs were taken in a barefoot condition and with high-heeled shoes. Lumbar lordosis was assessed by angle (Postural Analysis Software)	The UG had lower lordosis angles compared with the NUG. In the barefoot condition, the lumbar lordosis angle in the NUG decreases, whereas the UG increases. In the high-heeled condition, the lumbar lordosis angles in the UG increased and in the NUG decreases
Yang <i>et al</i> ^[23]	To analyze the correlation between cost density and cosmetic outcomes in the surgical treatment of AIS	Observational	<i>n</i> = 58 cases of IAS. Measurements: Photographic preoperative and follow-up and determination of cost. The scoliosis was assessed by angles (trunk shift and rib hump) and distances (waist line asymmetry) (Adobe Photoshop CS4)	On all post-operative photographic variables measured there was no statistically significant correlation between increasing cost density and change in cosmetic variables from pre-op to follow-up
Silveira <i>et al</i> ^[24]	To assess postural changes based on age and their association with the respiratory function in mouth breathing children	Observational	<i>n</i> = 17 nasal breathing and 17 mouth breathing children. The pulmonary function was assessed by forced spirometer. It was assessed the neck lordosis and lumbar lordosis angle (Fisiometer®3.0 Software)	Mouth-breathing children have neck hyperlordosis which increase with age, besides reduction in spirometry values. There was no difference in the lumbar lordosis between the groups
Iunes <i>et al</i> ^[25]	To analyze the efficacy of the Klapp method for treating scoliosis	Randomized clinical trial	<i>n</i> = 16 patients with scoliosis. The cervical lordosis, thoracic kyphosis and lumbar lordosis were assessed by angles (ALCimagem®-2000 software) before and after of treatment with 20 sessions of the Klapp method	Only the lumbar lordosis angle suffered modification post-intervention with Klapp method, with a trend to its decrease
Belli <i>et al</i> ^[26]	To assess the body posture of children with asthma compared to a non-asthmatic control group matched for gender, age, weight and height	Observational	<i>n</i> = 30 asthmatic children and 30 control group. The cervical lordosis, thoracic kyphosis and lumbar lordosis was assessed by angles (ALCimagem®-2000 software)	A significantly lower thoracic kyphosis angle value was observed in the asthmatic children. However, no significant differences were found between groups for the other angles
Chase <i>et al</i> ^[27]	To determine whether a sample of children and adolescents with STC had trunk musculoskeletal characteristics different from age- and sex-matched control subjects	Observational	<i>n</i> = 40 subjects with STC and 40 control subjects. The passive angle of the trunk flexion-extension was measured in the in prone-lying and trunk forward flexion and sagittal plane sitting posture was assessed by measurement of thoracolumbar flexion-extension angle (ImageJ Software)	There was no difference in spinal mobility between the two subject groups. The thoracolumbar flexion angle during sitting was statistically higher in the STC group than control group
Iunes <i>et al</i> ^[12]	To compare the agreement between the visual postural assessment carried out and the postural assessment carried out through computerized photogrammetry	Observational	<i>n</i> = 21. Evaluations: Visual postural assessment and computerized photogrammetry. In the photogrammetry, the cervical lordosis, thoracic kyphosis and lumbar lordosis were assessed by angles (ALCimagem®-2000 software)	For the cervical lordosis, thoracic kyphosis and lumbar lordosis it was not possible to compare the visual analysis with that from photogrammetry because there are not reports in the literature about normality values of the vertebral curvatures
Iunes <i>et al</i> ^[28]	To compare cervical spine alignment among individuals, with and without TMD	Observational	<i>n</i> = 90 (30 control group, 30 muscle signs and symptoms of TMD and 30 muscle signs and symptoms of TMD such as established diagnoses of dislocation and joint disorders). The cervical lordosis was assessed by angle (ALCimagem®-2000 software)	There were no differences among the three groups regarding cervical lordosis. The presence of TMD did not influence cervical posture, independent of TMD type or lack
Penha <i>et al</i> ^[29]	To quantitatively characterize spinal posture to verify any differences in the postural aspects analyzed and their possible correlation to sex or age in 7- and 8-year-old public school students in the city of Amparo, São Paulo, Brazil	Observational	<i>n</i> = 230 (115 in 7-year-old and 115 in 8-year-old). The thoracic kyphosis, lumbar lordosis and lateral spinal deviation were assessed by angles (CorelDraw v.11.0 software)	Only the group of 7-year-old boys showed lower angles in the lumbar lordosis from the other groups. In the thoracic kyphosis, there was a difference between the age groups, the 8-year-old children were more kyphotic than the 7-year-old. Eighty eight point seven percent of the children showed lateral spinal deviation. The most common side was to the left, the most frequent location was thoracic, and the proportion of the deviation was greater for boys (63%) than for girls (45%)

Rodrigues <i>et al</i> ^[30]	To measure the degree of thoracic kyphosis in older adult women with and without spinal osteoporosis and to verify the difference between the obtained values	Observational	<i>n</i> = 12 (6 women with a spinal osteoporosis and 6 women with a spinal osteopenia). The thoracic kyphosis was measured by angles (Autocad-2006)	The degree of thoracic kyphosis of the women with osteoporosis (66.8°) were higher when compared with the values of the women with osteopenia (53.0°)
Straker <i>et al</i> ^[31]	To evaluate the relationships between cervical, thoracic and lumbar sagittal sitting postures and adolescent prolonged NSP, with consideration of gender	Observational	<i>n</i> = 1593 adolescents. NSP was assessed by a questionnaire. It was assessed the cervicothoracic, lumbar and trunk angles in three static sitting postures: Looking straight ahead, looking down at their lap, and sitting slumped (Peak Motus motion analysis system v.8)	There were significant differences between gender in cervicothoracic, lumbar and trunk angles. Females showed more erect and lordotic postures when looking straight ahead. Adolescents with prolonged NSP sat with a more flexed cervicothoracic angle, a lower extended trunk angle, and a lower lordotic lumbar angle
Iunes <i>et al</i> ^[32]	To assess whether the frequency of high heel use has any influence on postural changes, and whether the type of high heel interferes in the posture	Observational	<i>n</i> = 40 (20 women that wore high-heeled shoes every day and 20 women that wore high heels occasionally to social functions). The subjects were photographed wore a two-piece swimsuit and no shoes. The cervical lordosis, thoracic kyphosis and lumbar lordosis were assessed by angles (ALCimagem® - 2000 software)	The frequency of use and type of high heel did not modify static posture in women
Smith <i>et al</i> ^[33]	(1) To determine whether photographic assessment could result in similar subgroups to previous, radiographically determined subgroups and clinically used subgroups of sagittal standing posture; (2) To explore the profiles of the clusters on gender, height and weight, and to explore the relationship of various spinal pain variables with identified clusters	Observational	<i>n</i> = 766 adolescents. Back pain experience was assessed by a questionnaire contained 130 questions. It was assessed the lumbar and trunk angle (Peak Motus motion analysis system)	Using 2-dimensional photographic images, the standing, sagittal thoraco-lumbo-pelvic alignment of adolescents can be classified into 4 groups: Neutral, sway, hyperlordotic, and flat. Adolescents classified as having non-neutral postures when compared with those classified as having a neutral posture demonstrated significantly higher odds for back pain ever
Yi <i>et al</i> ^[33]	To investigate the relationship between diaphragm excursion and spinal curvatures in mouth breathing children	Observational	<i>n</i> = 52 children (22 nose breathing group - control and 20 mouth breathing group). Images of diaphragm excursion were recorded using anteroposterior X-ray. The cervical lordosis, thoracic kyphosis and lumbar lordosis were assessed by angles (postural evaluation software-SAPO)	There is no relationship between spinal curvatures and diaphragm excursion in the groups studied
Min <i>et al</i> ^[34]	To describe the WBKA measured on preoperative clinical photographs and its significance in operative planning	Observational (retrospectively)	<i>n</i> = 11 patients who underwent lumbar spine osteotomy. The WBKA were measured in preoperative and at the last follow-up (mean 4 yr)	The average WBKA was 41 degrees (20 to 70 degrees) preoperatively and was 10.5 degrees (8 to 14 degrees) at the last follow up
Straker <i>et al</i> ^[35]	To test the hypothesis that the duration of computer use is associated with habitual postures in male and female adolescents	Observational	<i>n</i> = 884 adolescents. The computer use was assessed by questionnaire. The angles of thoracic flexion (line of C7 to T12 with respect to vertical), cervico-thoracic angle (angle between line of tragus to C7 and line of C7 to T12), trunk (angle between line of C7 to T12 and line of T12 to greater trochanter) and lumbar (angle between line of T12 to ASIS and line of ASIS to greater trochanter) were assessed in three sitting postures: Looking down, looking straight ahead and slumped position (Peak Motus motion analysis system)	Males - sitting looking straight ahead: no significant associations were observed between levels of computer use and variable postures. Males - sitting looking down: Significant but weak linear trend was observed, with thoracic flexion increasing with computer use. Females - sitting looking straight ahead: Increasing levels of computer use associated with increased lumbar lordosis. Females - sitting looking down: increasing levels of computer use associated with decreasing lumbar angle. Males and females - sitting slumped: Increasing of computer use associated with decreasing lumbar angle, only in females

Szopa <i>et al</i> ^[36]	To identify and define some compensatory postural patterns in children with CP in vertical positions	Observational	<i>n</i> = 18 children with CP. The angle of mechanical spinal axis deviation from the anatomical axis, the relation of the plumb line to the gluteal slitin was measured in these positions: Standing with both feet, and one (right and left) foot, two-knee kneeling, one-knee (right and left) kneeling and sitting (software manufactured by INFOMED)	Two main compensational postural patterns were distinguished on this basis in hemiparetic children, called antigravitational and progravitational posturing. The lateral curve of the spine in both types was directed towards the healthy body side, but in the antigravitational type the healthy side was the overloaded one, whereas in the progravitational type it was the unweighted one
Amsters <i>et al</i> ^[37]	To compare the posture of people with tetraplegia of short duration and long duration, in a static but functional position in a manual wheelchair	Observational	<i>n</i> = 30 people with tetraplegia; <i>n</i> = 30 control group. The thoracic kyphosis was assessed in sit posture in the wheelchair by chest angle	Significantly greater of the kyphosis thoracic were demonstrated for the tetraplegic group compared with able-bodied groups
O'Sullivan <i>et al</i> ^[38]	To examine whether a relationship exists between spinal posture and LBP in a specific sub-group of industrial workers who reported flexion-provoked pain	Observational	<i>n</i> = 21 control subjects and 24 LBP subjects. The low back pain was assessed by questionnaire. The lumbar lordosis was measured as the angle between the intersection of the tangents drawn through the T10/L2 markers and the L4/S2 markers. Positions: Natural sitting and maximal slumped sitting postures, natural standing and maximal sway standing postures, and lifting and maximal standing lumbar flexion postures (Scion Image analysis software)	No difference was observed between the two groups when comparing their "usual" sitting, standing and lifting lumbar flexion angles. When comparing the lumbar angle difference between "usual" sitting and maximal slumped sitting, the LBP group sat significantly closer to their end of range lumbar flexion in their "usual" sitting posture
Milosavljevic <i>et al</i> ^[39]	To determine whether adaptive postural and movement characteristics were evident in the thoracic and lumbar spine as well as the hips of shearers, and to determine whether any observed adaptive changes were associated with either current or previous LBP	Observational	<i>n</i> = 64 shearers and 64 non-shearers. Lumbar sagittal lordotic posture was determined by cord angular change between T12, L3 and the PSIS and it was expressed in radians per metre (rad/m). Mid-upper and mid-lower sagittal thoracic curves were also calculated and expressed in rad/m about the T1, T4, T8, and T4, T8, T12 respectively. Three positions were analyzed: Flexion, normal stance, extension (CAD program)	The mean value for lumbar extension for shearers (9.88) was significantly less than for non-shearers (14.08). Lumbar flexion demonstrated similar mean scores for both groups and no significant differences were noted. Lower thoracic curvature for shearers (2.14 rad/m) was significantly "flatter". than for nonshearers (2.48 rad/m). Comparisons of both lumbar lordosis as well as upper thoracic kyphosis did not demonstrate any significant differences between the two groups. In the non-shearing group, participants with previous LBP had significantly reduced ranges of lumbar extension and lumbar flexion. Shearers with previous LBP did not demonstrate any significant reduction of either of these ranges of lumbar motion. The mean lumbar extension in the non-shearing subgroup with previous LBP was still greater than that of the shearer group
Munhoz <i>et al</i> ^[40]	To investigate the relationship between internal derangements of the TMJ and body posture deviations	Observational	<i>n</i> = 50 (30 individuals with TMJ internal derangement and 20 control group). The cervical lordosis, thoracic kyphosis and lumbar lordosis were assessed by distances of the most prominent region until of the plumb line (CorelDraw v.9.0 software)	No statistically significant body postural differences between the groups were observed
Lima <i>et al</i> ^[41]	To determine and compare the posture of children with OMB and FMB in relation to NB children	Observational	<i>n</i> = 62 children (17 OMB group, 26 FMB group and 19 NB group). The cervical lordosis, thoracic kyphosis, lumbar lordosis and lateral deviation of the spine were assessed by angles (ALCimagem®-2000 software)	Significant alterations were observed in cervical straightening in the OMB group. Significant changes were observed in the thoracic kyphosis, indicating convexity in the OMB group. For the lumbar lordosis and lateral deviation of the spine, no significant alterations were observed in any of the groups

Raine <i>et al</i> ^[42]	To quantitatively describe the curvature of the thoracic spine in the sagittal plane	Observational	<i>n</i> = 160 asymptomatic men and women. The upper and lower thoracic kyphosis was assessed by the tangent angles in radians/mm between C7-T6 and T6-T12, respectively	Results of thoracic kyphosis were not shown
Christie <i>et al</i> ^[43]	To evaluate any static standing or sitting postural aberrations in chronic and acute low back pain patients in comparison with healthy individuals, in search of potential risk factors or associations for LBP	Observational	<i>n</i> = 59 (39 participants with LBP and 20 control group). Pain intensity was recorded using a VAS. The subjects were divided in acute and chronic pain. The lumbar lordosis and thoracic kyphosis was assessed by angles between C7-T12 and T12-L5, respectively, in standing and sitting positions	Standing positions: The chronic pain group had a significantly increased lordosis compared with the control group. The acute group had an increased kyphosis than the control group. Lumbar lordosis is the parameter most important in prediction of LBP group. Sitting positions: individuals with acute pain had an increased thoracic kyphosis. Thoracic kyphosis, indicated contribution to the prediction of study group
Watson ^[44]	To investigate possible relationships between the incidence of sports injury and the existence of body posture defects in football players	Observational	<i>n</i> = 52 football players (soccer, rugby, Gaelic football). The injuries were divided in four categories: Back injuries, knee injuries, ankle injuries and muscle strains. The assessment of the scoliosis, thoracic kyphosis and lumbar lordosis were not clear	Back injuries were associated with thoracic kyphosis, lumbar lordosis and scoliosis. Subjects who suffered from two, three or all four types of injuries had significantly lower scores for lordosis than subjects who sustained less than two types of injuries
Raine <i>et al</i> ^[45]	To identify gender differences in the thoracic kyphosis and to correlate thoracic kyphosis with head and shoulder position	Observational	<i>n</i> = 39. The upper (C7-T6) and lower (T6-T12) thoracic curvature were measured from the surface contour of the thoracic spine by the tangent angles in radians/cm (GTCO digitizer)	No significant difference between females and males for the measurement of upper thoracic, however the lower thoracic was significant higher in males. The sagittal plane head alignment was negatively correlated with upper thoracic curvature; there was increased curvature of the upper thoracic spine when the head was placed more anteriorly
Mitchell <i>et al</i> ^[46]	To report a new method of measuring the angle of curvature of the lumbar spine in pregnant women	Observational	<i>n</i> = 13 pregnant women. The lumbar lordosis was assessed by angle between T12-L1 and L5-S1	The degree of lumbar spine curvature in pregnant women was 33.9° (± 3.6°)
Dieck <i>et al</i> ^[47]	To examine the relationship between postural asymmetry and the subsequent development of back and neck pain	Observational	<i>n</i> = 903 women. Back and neck pain and risk factors were obtained by questionnaire. Deviation of the spine from de midline of the body to scoliosis measurement was assessed by angle	There was no evidence of a relationship between increasing midline deviation and subsequent low back pain

PAS: Postural Assessment Software; CP: Cerebral palsy; AIS: Adolescents idiopathic scoliosis; STC: Slow transit constipation; TMD: Temporomandibular disorder; UG: Users group; NUG: Nonuser group; NSP: Neck/shoulder pain; WBKA: Whole body kyphosis angle; LBP: Low back pain; TMJ: Temporomandibular Joint; OMB: Obstructive mouth breathing; FMB: Functional mouth breathing; NB: Nasal breathing; VAS: Visual analogue scale.

the samples comprise patients with asthma^[15,26], tetraplegia^[37], cerebral palsy^[16,36] temporomandibular joint dysfunction^[28,40], osteoporosis and osteopenia^[30], low back pain^[38,43], slow transit constipation^[27] and children with mouth breathing^[21,24,33,41].

With regard to the region of the spine evaluated, greater difficulty has been documented in evaluating the sagittal plane compared to the frontal plane. This may be explained by the fact that, in the frontal plane, symmetry between the right and left sides and straightness of the spine can be expected^[6,12]. By contrast, in the sagittal plane, the spine presents physiological curvatures and changes characterized by an increase or decrease in the magnitude of the curvatures^[50], which hinders visual and subjective evaluation. In an attempt to quantify the magnitude of the curvatures, various mathematical procedures have been proposed for evaluating the

sagittal curvature of the spine. Possibly for this reason, about 80% of the studies found in this systematic review attempted to evaluate cervical lordosis, thoracic kyphosis and lumbar lordosis, while only eight articles evaluated the existence of scoliosis^[16,17,23,29,36,41,44,47].

Nevertheless, in the literature, there is still a need for postural evaluation software that can be used to do more than quantify joint angles and the distances between the segments, which, in addition can, be used to provide a diagnostic classification of changes in the magnitudes of the spine in individuals. To achieve this, normality values of body segments need to be established in the literature. However, regarding the spine, there is some controversy in relation to the reference values for the angles of curvature in the sagittal plane in the ideal alignment^[12].

The data collection protocols in the studies using

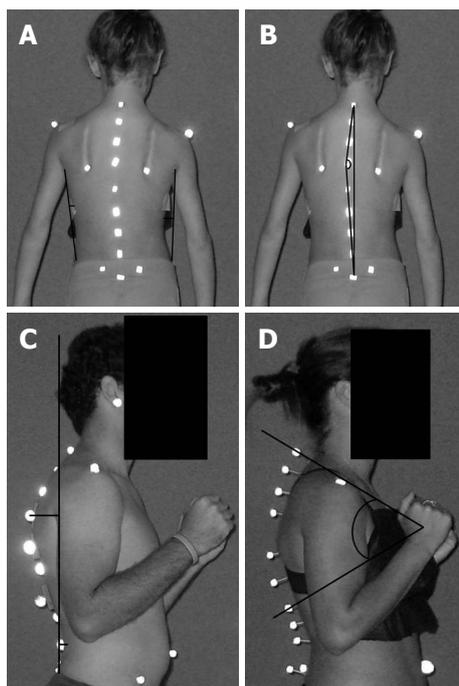


Figure 2 Examples of the techniques used to measure spinal curvature found in the articles composing the present systematic review. A: Linear values for scoliosis evaluation^[23]; B: Angular values for scoliosis evaluation^[17]; C: Linear values for thoracic and lumbar curvatures^[21]; D: Angular values for thoracic curvature^[30]. The images used are illustrations prepared for the present study.

photogrammetry as an evaluation tool tend to be very similar, differing minimally according to the purpose of each evaluation. All the methods are based on basic procedures such as: (1) preliminary preparation of the collection location with standardized location of the camera and the subject; (2) palpation and marking of anatomical reference points; and (3) photographic records of individuals in certain positions^[2,8,9,45].

However, concerning the data analysis procedures, various software and digital routines are used for scanning anatomical landmarks. Similarly, the mathematical procedures adopted in software or digital routines are very different^[51]. Nevertheless, in most cases, the studies do not provide information on the mathematical procedures adopted in the software or in digital routines that support the evaluation results. Allied to this, in some cases the software is not freely available, which makes it difficult to reproduce the evaluation method in other studies.

Therefore, we emphasize the wide divergence of software and mathematical procedures found in this review. Among the known and validated software packages used repeatedly in the selected articles are ALCimager®-2000^[12,25,26,28,32,41], Postural Assessment Software (PAS)^[15,19,21,22,33], Peak Motus Motion Analysis System^[3,31,35], CorelDraw^[29,40], AutoCad^[16,30] and Image J Software^[8,27].

As regards the various mathematical routines embedded in these systems, angular and linear values have been the most widely used to measure alterations of the

spine in the frontal and sagittal planes, *i.e.*, to determine the magnitudes of scoliosis and anteroposterior curvatures, respectively. Figure 2 illustrates some of the techniques used to measure the spinal alterations.

The angular values are often used, since the gold standard of postural assessment uses an angular calculation to measure the degree of scoliosis and the magnitude of the sagittal curvature of the spine. In other words, in the X-ray examination of the spine it is possible to calculate the so-called Cobb angle, which is widely used for diagnosis of spinal posture^[52].

Some of the selected studies evaluate the angles of scoliosis using photogrammetry in a similar way to the Cobb angle^[17,23]. However, while the Cobb angle uses the vertebral bodies for evaluation, photogrammetry calculates the magnitude of the curve through the spinal processes of the vertebrae of interest. For this evaluation, two lines are drawn joining the spinous processes and the angle between these lines gives the angle of curvature^[17,23].

The linear values in the frontal plane are established according to the statement that the spine should be a straight line^[6]. Hence, methodologies calculate postural alteration by the degree to which marked points, referring to the spinous processes, deviate from the vertical line^[23,29,36,47].

In the sagittal plane, angular values are more often used than linear values for evaluating the anteroposterior curvatures of the spine.

Similar to the Cobb angle, photogrammetry is recommended for use in evaluating the spinal curvature based on the calculation of the angle between two points on the spine^[30,43,46]. However, it uses the spinous processes as a reference, while radiography uses the vertebral bodies.

Nevertheless, it should be noted that the spinous processes have an angle of inclination in relation to the vertebral body^[53] and that this angle may interfere with obtaining the angle of curvature by photogrammetry. Thus, caution is recommended when using a similar method to the gold standard in the mathematical procedures of postural evaluation software, since palpated anatomical landmark and used with reference is totally different.

When the photogrammetric evaluation software resembles the way of measuring the magnitude of the curves, they diverge in relation to vertebral levels used or anatomical landmarks. When distinct marked points are used, the calculation of curvatures will be modified, making it difficult to compare studies. In the studies included in this systematic review, some vertebral levels reported for thoracic kyphosis were between: C7-T12^[43], T1-T4-T8^[39], T4-T8-T12^[39] and T1-T6-T12^[20]. For lumbar lordosis they were between T12-L5^[43], T12-Anterior superior iliac spine - femur greater trochanter^[3,31,35].

Besides the similarity with the calculation of Cobb angle, some recurring angular values were calculated angles for the three curvatures: (1) cervical lordosis: the union of three lines passing through occipital, C4

and C7 until a later vertical line; (2) thoracic kyphosis: The union of three lines passing through C7, T7 and T12 until a posterior-vertical line; and (3) lumbar lordosis: Union of three lines passing through T12, L3 and L5 posterior to a vertical line^[12,22,25,26,28]. Among these possibilities for measuring sagittal curvature, routines based on other types of calculations were also found, such as the curvatures of the contour tangent^[38,42,45], torso angle^[3,16,31,35], and chest angle^[37].

According to the theories that use linear values to evaluate the spine in the sagittal plane, alterations in the curvature can be quantified by measuring the distance from the spinous process to a vertical reference line. In rectified curvatures, the distances decrease, while in increased curvatures the distances increase^[6].

Despite the wide range of mathematical procedures that can be used to quantitatively evaluate the spine, inserted in photogrammetry, in clinical practice and research, health professionals and students are often faced with a scarcity of tools that allow them to classify an individual's posture. In other words, the angular or linear results provided by software often lack clinical significance because they are not equivalent to the gold standard. Thus, the benefits, limitations, target audience, and use characteristics of photogrammetry need to be carefully considered when selecting the software and/or mathematical procedure in order to facilitate the correct choice of evaluation methodology for different situations, both in clinical and in scientific research.

The present systematic review shows that photogrammetry can be widely used in the scientific research environment, because it facilitates the collection and analysis of detailed data, thus permitting assessment not only of the spine but also of other body segments in both the sagittal and frontal planes. On the other hand, in the school environment, data collection should prioritize simplified protocols, thus facilitating the assessment of large populations. Moreover, the software and mathematical procedures for the postural analysis should be easily available, as are PAS and ALCimager[®]-2000. In the clinical environment, the choice of photogrammetric data collection and of the assessment protocol will depend on the purpose of the postural evaluation, as well as the health professional's investigative focus, so that a simplified or more complete assessment protocol can be used.

A wide range of studies was found to use photogrammetry as a tool for non-invasive evaluation of the spine, both for measurement of anteroposterior and lateral alterations. However, most of the selected articles were observational studies, only one being a randomized clinical trial.

Yet, it was also observed that, although the data collection methodologies used are similar across the studies, they are very different concerning aspects of data analysis, especially with regard to the mathematical routines that support the different software packages for postural evaluation. Finally, even though photo-

grammetry is a viable, valid and reproducible option for the evaluation of the spine, there is still a lack of studies in the literature showing software whose results provide both the magnitude of the curvatures and the diagnostic classification of the posture of the spine, certified with clinical significance.

COMMENTS

Background

Photogrammetry is a widely used non-invasive technique for measuring aspects of the spine for the purpose of postural evaluation. Its use undoubtedly contributes to reducing exposure to radiation and thus enables the monitoring of postural treatment. However, the application of this technique in postural evaluation is directly dependent on both the collection procedures and the mathematical methods used to provide measurements and postural diagnoses. Although the use of photogrammetry in spinal evaluation is widespread, its applicability may be questioned, as it remains unclear how this technique is being used to monitor postural treatment or to map attitudes among populations in observational studies.

Research frontiers

Essentially, the problem is two different researchers can look at the same image and arrive at different conclusions regarding diagnosis because they use distinct mathematical methods. Hence, there is a need to identify the best method of using photogrammetry to accurately measure spinal curvatures.

Innovations and breakthroughs

To be best of the authors' knowledge there is no systematic review which brings together the protocols and mathematical methods involved when it is applied in the assessment of spinal posture. Hence, the aim of this study is to present, in a concise way, the articles dealing with the application of photogrammetry in postural evaluation, so researchers can more easily discuss the suitability of the procedures currently being applied.

Applications

With photogrammetry, the aim of the assessment, whether it is for clinical, research or collective health purposes, must be considered when choosing which protocol to use to evaluate spinal posture. When using photogrammetry in scientific research, a protocol or software that provides detailed postural analysis should be the first choice. In the clinical environment, the choice of protocol will depend on the objectives established for the patient by the physiotherapist. When dealing with a collective health situation, such as groups of schoolchildren, it is necessary to prioritize simpler protocols.

Terminology

Photogrammetry: Is the technique of determining measurements based on photographs. The Cobb angle: Is used to measure the spinal curvatures, defined as the angle formed between a line drawn parallel to the superior endplate of one vertebra above the curvature and a line drawn parallel to the inferior endplate of the vertebra one level below the curvature.

Peer-review

This article demonstrates an in-depth review of the available literature on the application of photogrammetry in postural evaluation.

REFERENCES

- 1 Carman DL, Browne RH, Birch JG. Measurement of scoliosis and kyphosis radiographs. Intraobserver and interobserver variation. *J Bone Joint Surg Am* 1990; **72**: 328-333 [PMID: 2312528]
- 2 Dunk NM, Lalonde J, Callaghan JP. Implications for the use of postural analysis as a clinical diagnostic tool: reliability of quantifying upright standing spinal postures from photographic images. *J Manipulative Physiol Ther* 2005; **28**: 386-392 [PMID: 16096037 DOI: 10.1016/j.jmpt.2005.06.006]

- 3 **Smith A**, O'Sullivan P, Straker L. Classification of sagittal thoraco-lumbo-pelvic alignment of the adolescent spine in standing and its relationship to low back pain. *Spine* (Phila Pa 1976) 2008; **33**: 2101-2107 [PMID: 18758367 DOI: 10.1097/BRS.0b013e31817ec3b0]
- 4 **Fortin C**, Feldman DE, Cheriet F, Gravel D, Gauthier F, Labelle H. Reliability of a quantitative clinical posture assessment tool among persons with idiopathic scoliosis. *Physiotherapy* 2012; **98**: 64-75 [PMID: 22265387 DOI: 10.1016/j.physio.2010.12.006]
- 5 **D'osualdo F**, Schierano S, Cisotti C. The evaluation of the spine through the surface: The role of surface measurements in the evaluation and treatment of spine diseases in young patients. *Eura Medicophys* 2002; **38**: 147-152
- 6 **Furlanetto TS**, Candotti CT, Comerlato T, Loss JF. Validating a postural evaluation method developed using a Digital Image-based Postural Assessment (DIPA) software. *Comput Methods Programs Biomed* 2012; **108**: 203-212 [PMID: 22522063 DOI: 10.1016/j.cmpb.2012.03.012]
- 7 **Masso PD**, Gorton GE. Quantifying changes in standing body segment alignment following spinal instrumentation and fusion in idiopathic scoliosis using an optoelectronic measurement system. *Spine* (Phila Pa 1976) 2000; **25**: 457-462 [PMID: 10707391 DOI: 10.1097/00007632-200002150-00011]
- 8 **Edmondston SJ**, Christensen MM, Keller S, Steigen LB, Barclay L. Functional radiographic analysis of thoracic spine extension motion in asymptomatic men. *J Manipulative Physiol Ther* 2012; **35**: 203-208 [PMID: 22386914 DOI: 10.1016/j.jmpt.2012.01.008]
- 9 **Letafatkar A**, Amirsasan R, Abdolvahabi Z, Hadadnezhad M. Reliability and validity of the AutoCAD software method in lumbar lordosis measurement. *J Chiropr Med* 2011; **10**: 240-247 [PMID: 22654681 DOI: 10.1016/j.jcm.2011.02.003]
- 10 **Leroux MA**, Zabjek K, Simard G, Badeaux J, Coillard C, Rivard CH. A noninvasive anthropometric technique for measuring kyphosis and lordosis: an application for idiopathic scoliosis. *Spine* (Phila Pa 1976) 2000; **25**: 1689-1694 [PMID: 10870144 DOI: 10.1097/00007632-200007010-00012]
- 11 **van Niekerk SM**, Louw Q, Vaughan C, Grimmer-Somers K, Schreive K. Photographic measurement of upper-body sitting posture of high school students: a reliability and validity study. *BMC Musculoskelet Disord* 2008; **9**: 113 [PMID: 18713477 DOI: 10.1186/1471-2474-9-113]
- 12 **Iunes DH**, Bevilaqua-Grossi D, Oliveira AS, Castro FA, Salgado HS. Comparative analysis between visual and computerized photogrammetry postural assessment. *Braz J Phys Ther* 2009; **13**: 308-315 [DOI: 10.1590/S1413-35552009005000039]
- 13 **Higgins JPT**, Green S. *Cochrane handbook for systematic reviews of interventions*. 2014. Available from: URL: <http://handbook.cochrane.org/v5.0.2/>
- 14 **Downs SH**, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; **52**: 377-384 [PMID: 9764259 DOI: 10.1136/jech.52.6.377]
- 15 **Almeida VP**, Guimarães FS, Moço VJ, Menezes SL, Mafort TT, Lopes AJ. [Correlation between pulmonary function, posture, and body composition in patients with asthma]. *Rev Port Pneumol* 2013; **19**: 204-210 [PMID: 23746425 DOI: 10.1016/j.rppneu.2013.03.004]
- 16 **Cheng HY**, Lien YJ, Yu YC, Ju YY, Pei YC, Cheng CH, Wu DB. The effect of lower body stabilization and different writing tools on writing biomechanics in children with cerebral palsy. *Res Dev Disabil* 2013; **34**: 1152-1159 [PMID: 23376050 DOI: 10.1016/j.ridd.2012.12.019]
- 17 **Fortin C**, Ehrmann Feldman D, Cheriet F, Labelle H. Differences in standing and sitting postures of youth with idiopathic scoliosis from quantitative analysis of digital photographs. *Phys Occup Ther Pediatr* 2013; **33**: 313-326 [PMID: 23298337 DOI: 10.3109/01942638.2012.747582]
- 18 **Annetts S**, Coales P, Colville R, Mistry D, Moles K, Thomas B, van Deursen R. A pilot investigation into the effects of different office chairs on spinal angles. *Eur Spine J* 2012; **21** Suppl 2: S165-S170 [PMID: 22349969 DOI: 10.1007/s00586-012-2189-z]
- 19 **Weber P**, Corrêa ECR, Milanese JM, Soares JC, Trevisa ME. Craniocervical posture: cephalometric and biophotogrammetric analysis. *Braz J Oral Sci* 2012; **11**: 416-421
- 20 **Edmondston SJ**, Waller R, Vallin P, Holthe A, Noebauer A, King E. Thoracic spine extension mobility in young adults: influence of subject position and spinal curvature. *J Orthop Sports Phys Ther* 2011; **41**: 266-273 [PMID: 21335925 DOI: 10.2519/jospt.2011.3456]
- 21 **Milanese JM**, Borin G, Corrêa EC, da Silva AM, Bortoluzzi DC, Souza JA. Impact of the mouth breathing occurred during childhood in the adult age: biophotogrammetric postural analysis. *Int J Pediatr Otorhinolaryngol* 2011; **75**: 999-1004 [PMID: 21632123 DOI: 10.1016/j.ijporl.2011.04.018]
- 22 **de Oliveira Pezzan PA**, João SM, Ribeiro AP, Manfio EF. Postural assessment of lumbar lordosis and pelvic alignment angles in adolescent users and nonusers of high-heeled shoes. *J Manipulative Physiol Ther* 2011; **34**: 614-621 [PMID: 22078999 DOI: 10.1016/j.jmpt.2011.09.006]
- 23 **Yang S**, Jones-Quaidoo SM, Eager M, Griffin JW, Reddi V, Novicoff W, Shilt J, Bersusky E, Defino H, Ouellet J, Arlet V. Right adolescent idiopathic thoracic curve (Lenke 1 A and B): does cost of instrumentation and implant density improve radiographic and cosmetic parameters? *Eur Spine J* 2011; **20**: 1039-1047 [PMID: 21519929 DOI: 10.1007/s00586-011-1808-4]
- 24 **Silveira Wd**, Mello FC, Guimarães FS, Menezes SL. Postural alterations and pulmonary function of mouth-breathing children. *Braz J Otorhinolaryngol* 2010; **76**: 683-686 [PMID: 21180932 DOI: 10.1590/S1808-86942010000600002]
- 25 **Iunes DH**, Cecílio MB, Dozza MA, Almeida PR. Quantitative photogrammetric analysis of the Klapp method for treating idiopathic scoliosis. *Rev Bras Fisioter* 2010; **14**: 133-140 [PMID: 20464171 DOI: 10.1590/S1413-35552010005000009]
- 26 **Belli JF**, Chaves TC, de Oliveira AS, Grossi DB. Analysis of body posture in children with mild to moderate asthma. *Eur J Pediatr* 2009; **168**: 1207-1216 [PMID: 19132386 DOI: 10.1007/s00431-008-0911-y]
- 27 **Chase JW**, Stillman BC, Gibb SM, Clarke MC, Robertson VJ, Catto-Smith AG, Hutson JM, Southwell BR. Trunk strength and mobility changes in children with slow transit constipation. *J Gastroenterol Hepatol* 2009; **24**: 1876-1884 [PMID: 19686406 DOI: 10.1111/j.1440-1746.2009.05940.x]
- 28 **Iunes DH**, Carvalho LCF, Oliveira AS, Bevilaqua-Grossi D. Craniocervical posture analysis in patients with temporomandibular disorder. *Braz J Phys Ther* 2009; **13**: 89-95 [DOI: 10.1590/S1413-35552009005000011]
- 29 **Penha PJ**, Baldini M, João SM. Spinal postural alignment variance according to sex and age in 7- and 8-year-old children. *J Manipulative Physiol Ther* 2009; **32**: 154-159 [PMID: 19243728 DOI: 10.1016/j.jmpt.2008.12.009]
- 30 **Rodrigues ACC**, Romeiro CAP, Patrizzi LJ. Evaluation of thoracic kyphosis in older adult women with osteoporosis by means of computerized biophotogrammetry. *Braz J Phys Ther* 2009; **13**: 205-209 [DOI: 10.1590/S1413-35552009005000036]
- 31 **Straker LM**, O'Sullivan PB, Smith AJ, Perry MC. Relationships between prolonged neck/shoulder pain and sitting spinal posture in male and female adolescents. *Man Ther* 2009; **14**: 321-329 [PMID: 18555730 DOI: 10.1016/j.math.2008.04.004]
- 32 **Iunes DH**, Monte-Raso VV, Santos CBA, Castro FA, Salgado HS. Postural influence of high heels among adult women: analysis by computerized photogrammetry. *Braz J Phys Ther* 2008; **12**: 454-459 [DOI: 10.1590/S1413-35552008005000003]
- 33 **Yi LC**, Jardim JR, Inoue DP, Pignatari SS. The relationship between excursion of the diaphragm and curvatures of the spinal column in mouth breathing children. *J Pediatr* (Rio J) 2008; **84**: 171-177 [PMID: 18372937 DOI: 10.2223/JPED.1771]
- 34 **Min K**, Hahn F, Leonardi M. Lumbar spinal osteotomy for kyphosis in ankylosing spondylitis: the significance of the whole body kyphosis angle. *J Spinal Disord Tech* 2007; **20**: 149-153 [PMID: 17414985 DOI: 10.1097/01.bsd.0000211252.67576.d9]
- 35 **Straker LM**, O'Sullivan PB, Smith A, Perry M. Computer use and

- habitual spinal posture in Australian adolescents. *Public Health Rep* 2007; **122**: 634-643 [PMID: 17877311]
- 36 **Szopa A**, Domagalska M, Czupryna K, Plaszewski M. Postural consequences of muscle tone disorders in children with cerebral palsy (hemiparesis). *Fizioter* 2007; **3**: 241-249
- 37 **Amsters D**, Nitz J. The consequences of increasing age and duration of injury upon the wheelchair posture of men with tetraplegia. *Int J Rehabil Res* 2006; **29**: 347-349 [PMID: 17106355 DOI: 10.1097/MRR.0b013e328010f540]
- 38 **O'Sullivan PB**, Dankaerts W, Burnett AF, Garreth TF, Jefford E, Naylor CS, O'Sullivan KJ. Effect of different upright sitting postures on spinal- pelvic curvature and trunk muscle activation in a pain-free population. *Spine* 2006; **31**: E707-E712
- 39 **Milosavljevic S**, Milburn PD, Knox BW. The influence of occupation on lumbar sagittal motion and posture. *Ergonomics* 2005; **48**: 657-667 [PMID: 16087500 DOI: 10.1080/00140130500070848]
- 40 **Munhoz WC**, Marques AP, de Siqueira JT. Evaluation of body posture in individuals with internal temporomandibular joint derangement. *Cranio* 2005; **23**: 269-277 [PMID: 16353467]
- 41 **Lima LC**, Baraúna MA, Sologurem MJ, Canto RS, Gastaldi AC. Postural alterations in children with mouth breathing assessed by computerized biophotogrammetry. *J Appl Oral Sci* 2004; **12**: 232-237 [PMID: 21049259 DOI: 10.1590/S1678-77572004000300014]
- 42 **Raine S**, Twomey LT. Head and shoulder posture variations in 160 asymptomatic women and men. *Arch Phys Med Rehabil* 1997; **78**: 1215-1223 [PMID: 9365352]
- 43 **Christie HJ**, Kumar S, Warren SA. Postural aberrations in low back pain. *Arch Phys Med Rehabil* 1995; **76**: 218-224 [PMID: 7717811 DOI: 10.1016/S0003-9993(95)80604-0]
- 44 **Watson AW**. Sports injuries in footballers related to defects of posture and body mechanics. *J Sports Med Phys Fitness* 1995; **35**: 289-294 [PMID: 8776077]
- 45 **Raine S**, Twomey L. Posture of the head, shoulders and thoracic spine in comfortable erect standing. *Aust J Physiother* 1994; **40**: 25-32 [PMID: 25026488 DOI: 10.1016/S0004-9514(14)60451-7]
- 46 **Mitchell J**, Ness D. A new method of measuring the degree of lumbar spine curvature in pregnant women. *Physiotherapy* 1992; **48**: 51-54
- 47 **Dieck GS**, Kelsey JL, Goel VK, Panjabi MM, Stephen WD, Laprade MH. An epidemiologic study of the relationship between postural asymmetry in the teen years and subsequent back and neck pain. *Spine* 1985; **10**: 872-877
- 48 **de Oliveira TS**, Candotti CT, La Torre M, Pelinson PP, Furlanetto TS, Kutchak FM, Loss JF. Validity and reproducibility of the measurements obtained using the flexicurve instrument to evaluate the angles of thoracic and lumbar curvatures of the spine in the sagittal plane. *Rehabil Res Pract* 2012; **2012**: 186156 [PMID: 22619723 DOI: 10.1155/2012/186156]
- 49 **Hanna T**. What is somatics? Somatics. *Novato Institute for Somatic Research and Training* 1986; **5**: 4-8
- 50 **Singh DK**, Bailey M, Lee R. Biplanar measurement of thoracolumbar curvature in older adults using an electromagnetic tracking device. *Arch Phys Med Rehabil* 2010; **91**: 137-142 [PMID: 20103408 DOI: 10.1016/j.apmr.2009.08.145]
- 51 **Fortin C**, Feldman DE, Cheriet F, Labelle H. Validity of a quantitative clinical measurement tool of trunk posture in idiopathic scoliosis. *Spine (Phila Pa 1976)* 2010; **35**: E988-E994 [PMID: 20700086 DOI: 10.1097/BRS.0b013e3181cd2cd2]
- 52 **Mac-Thiong JM**, Pinel-Giroux FM, de Guise JA, Labelle H. Comparison between constrained and non-constrained Cobb techniques for the assessment of thoracic kyphosis and lumbar lordosis. *Eur Spine J* 2007; **16**: 1325-1331 [PMID: 17426991 DOI: 10.1007/s00586-007-0314-1]
- 53 **Gilad I**, Nissan M. Sagittal evaluation of elemental geometrical dimensions of human vertebrae. *J Anat* 1985; **143**: 115-120 [PMID: 3870717]

P- Reviewer: Bicanic G, Robertson GA **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Liu SQ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 March 18; 7(3): 149-201



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

EDITORIAL

- 149 Induced pluripotent stem cells in cartilage repair
Lietman SA
- 156 Evidence base and future research directions in the management of low back pain
Abbott A
- 162 New regulations for medical devices: Rationale, advances and impact on research and patient care
Labek G, Schöffl H, Stoica CI
- 167 Entrapment of middle cluneal nerves as an unknown cause of low back pain
Aota Y

REVIEW

- 171 Major osteoporotic fragility fractures: Risk factor updates and societal impact
Pisani P, Renna MD, Conversano F, Casciaro E, Di Paola M, Quarta E, Muratore M, Casciaro S

MINIREVIEWS

- 182 Injuries in jumpers - are there any patterns?
Rocos B, Chesser TJ

ORIGINAL ARTICLE

Retrospective Study

- 188 Outcomes of tenodesis of the long head of the biceps tendon more than three months after rupture
McMahon PJ, Speziali A
- 195 Knee awareness and functionality after simultaneous bilateral vs unilateral total knee arthroplasty
Latifi R, Thomsen MG, Kallemose T, Husted H, Troelsen A

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Florian M Kovar, MD, Doctor, Department for Trauma Surgery, General Hospital Vienna, Medical University Vienna, 1180 Vienna, Austria

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Dan Li*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Xue-Mei Gong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLICATION DATE
 March 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION
<http://www.wjnet.com/esps/>

Induced pluripotent stem cells in cartilage repair

Steven A Lietman

Steven A Lietman, Cleveland Clinic Departments of BME and Orthopaedics, Cleveland Clinic Foundation, Cleveland, OH 44195, United States

Author contributions: Lietman SA solely contributed to this paper.

Conflict-of-interest statement: The author certifies that he has no commercial associations (*e.g.*, consultancies, stock ownership, equity interest, patent/licensing arrangements, *etc.*) that might pose a conflict of interest in connection with the submitted article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Steven A Lietman, MD, Cleveland Clinic Departments of BME and Orthopaedics, Cleveland Clinic Foundation, 9500 Euclid Ave, Desk A41, Cleveland, OH 44195, United States. lietmas@ccf.org
Telephone: +1-216-4452742
Fax: +1-216-4456255

Received: June 30, 2015

Peer-review started: July 3, 2015

First decision: October 13, 2015

Revised: December 1, 2015

Accepted: December 29, 2015

Article in press: January 4, 2016

Published online: March 18, 2016

Abstract

Articular cartilage repair techniques are challenging. Human embryonic stem cells and induced pluripotent stem cells (iPSCs) theoretically provide an unlimited number of specialized cells which could be used in articular cartilage repair. However thus far chondrocytes

from iPSCs have been created primarily by viral transfection and with the use of cocultured feeder cells. In addition chondrocytes derived from iPSCs have usually been formed in condensed cell bodies (resembling embryoid bodies) that then require dissolution with consequent substantial loss of cell viability and phenotype. All of these current techniques used to derive chondrocytes from iPSCs are problematic but solutions to these problems are on the horizon. These solutions will make iPSCs a viable alternative for articular cartilage repair in the near future.

Key words: Induced pluripotent stem cells; Articular cartilage; Cartilage repair; Stem cells

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Herein we review the challenges in articular cartilage repair. Further we explain that induced pluripotent stem cells (iPSCs) represent an exciting theoretically limitless source of autologous cells for articular cartilage repair. We also discuss a novel systematic approach to optimally derive articular chondrocytes from iPSCs.

Lietman SA. Induced pluripotent stem cells in cartilage repair. *World J Orthop* 2016; 7(3): 149-155 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/149.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.149>

INTRODUCTION

Nearly 1 in 2 people develop symptomatic knee osteoarthritis (OA) by age 85 years, two in three people who are obese develop symptomatic knee OA in their lifetime^[1], and 1 in 4 people develop painful hip arthritis in their lifetime^[2]. Over 30 million Americans suffer from arthritis and other rheumatic conditions that affect joint and connective tissue; and by 2030 nearly 25% of the American

population is expected to be affected by such conditions^[3]. Joint Replacement.

Perhaps as a result or as a testament to the inability of articular cartilage to heal, knee replacement is now the most common elective surgery in the United States (Figure 1). Knee replacement though is not appropriate for young patients as it only lasts for an average of 15 years^[4] so alternative cellular treatments for osteoarthritis have been sought.

Articular cartilage is made up of cells (5%) with extracellular matrix and water (95%)^[5]. Articular chondrocytes express high levels of COL2A1, SOX9 and AGGRECAN^[6]. Endogenous attempts at cartilage repair are ineffective in composition (primarily creating fibrocartilage with type I rather than type II collagen) and the reparative tissue does not provide durable healing to the adjacent normal cartilage Figure 1^[6]. During embryonic cartilage formation, mesenchymal condensation is the prerequisite for the induction of chondrogenesis. Initiation of limb development starts with the lateral plate mesodermal cells, which proliferate, aggregate and form mesenchymal condensations^[7]. These primordial cells differentiate into chondrocytes and form cartilage anlagen^[7-10].

One major limitation when studying primary chondrocytes in culture is their loss of phenotype^[11]. Research in cell-based cartilage tissue engineering has focused on identifying a cell source suitable for regenerating cartilage. Mesenchymal stem cells (MSCs) would seem to be well suited for tissue engineering and are multipotent cells able to differentiate into chondrocytes, osteoblasts, adipocytes and myocytes^[12-15]. However, even though MSCs can be easily obtained from bone marrow, fat and skin, these primary cells have limited proliferation capacity when cultured *in vitro* and relatively low numbers of MSCs are capable of chondrocyte differentiation^[16-21]. Autologous chondrocytes and MSCs have still been used in regeneration of articular cartilage^[22-24]. However there are limitations in terms of the ability of adult differentiated chondrocytes to heal a cartilage defect, the numbers of cells that can be obtained using these autologous cells due to their obscurity, and due to the limited maintenance of their phenotype with cell division^[16]. The only exception to the inability of a cartilage defect to heal effectively and seamlessly appears to be in a fetal lamb model in which partial thickness articular cartilage defects did heal to subsequently normal appearing cartilage^[25].

As a result our group and others have become interested in the use of induced pluripotent stem cells (iPSCs) that can be derived from a patient skin biopsy, transformed into iPSCs and then into articular chondrocytes with theoretically large numbers of cells without the concerns of disease transmission from allogeneic cell transfer. In this review we will discuss the current status and recent progress in the development of articular chondrocytes from iPSCs.

DEVELOPMENT OF IPSCS

Many attempts have been made in the last decade

to obtain various MSCs, derived from iPSCs, in ample quantity and high purity after differentiation *in vitro*^[26-33]; and the International Society for Cellular Therapy has defined three primary criteria for cells to meet the definition of MSCs. First, MSCs must be plastic-adherent when maintained in standard culture conditions. Second, MSCs must express CD105, CD73 and CD90, and lack expression of CD45, CD34, CD14, CD11b, CD79alpha or CD19 and HLA-DR surface molecules. Third, MSCs must be able to differentiate into osteoblasts, adipocytes and chondrogenic cells *in vitro*^[34]. In the past, undifferentiated iPSCs have contaminated the differentiated population of MSCs, and they can contribute to teratoma tumor formation; and a uniformly differentiated cell population is necessary for clinical use^[35]. iPSCs were developed by Yamanaka by taking differentiated cells and reprogramming them to an embryonic-like state by transfer of nuclear contents into oocytes or by fusion with cells. Specifically he demonstrated induction of pluripotent stem cells from mouse adult fibroblasts by introducing four factors, Oct3/4, Sox2, c-Myc, and Klf4, under ES cell culture conditions^[36,37]. These cells, which his group designated iPSCs, exhibit the morphology and growth properties of ES cells and express ES cell marker genes. Subcutaneous transplantation of these iPSCs into nude mice resulted in tumors containing a variety of tissues from all three germ layers. Their work demonstrated that pluripotent stem cells could be directly generated from fibroblast cultures by the addition of only a few defined factors^[38].

The fibroblasts used to derive iPSCs can be obtained from a skin punch biopsy done in clinic at the time of patient presentation. iPSCs have the potential to self-renew and differentiate into many adult cell types^[39] and represent a theoretically nearly unlimited supply of cells for studying normal cell function and modeling of disease^[16,17,27,31,40]. More recent publications have proven the beneficial effect of cells derived from stem cells^[41,42]. Stem cell derived cardiomyocytes improve myocardial performance in animal models^[42]; and stem cells derived from neuroprogenitor cells lead to regeneration of functional neurons in *in vivo* models^[4,43]. Stem cells derived from retinal epithelial cells improve vision in rodents and humans^[33,44]. iPSCs, also potentially provide cell sources for the development of regenerative therapy in articular cartilage repair^[45-48]. The chondrogenic cells derived from iPSCs are similar to the fetal lamb chondrocytes, (effectively able to repair cartilage) based on their rapid proliferation and ability to make healthy appearing tissue^[38,47-51]. iPSCs can also be manipulated to correct genetic defects, a very important consideration for genetically inherited diseases, including RA. Genetic manipulations could indeed allow *de novo* produced articular cells to be resistant to inflammatory stimuli and to produce tissues insensitive to degrading enzymes. Based on these considerations and evidence that human iPSCs can be directed to undergo differentiation into various cell types, iPSCs are currently the best option to develop strategies for tissue repair in articular cartilage.

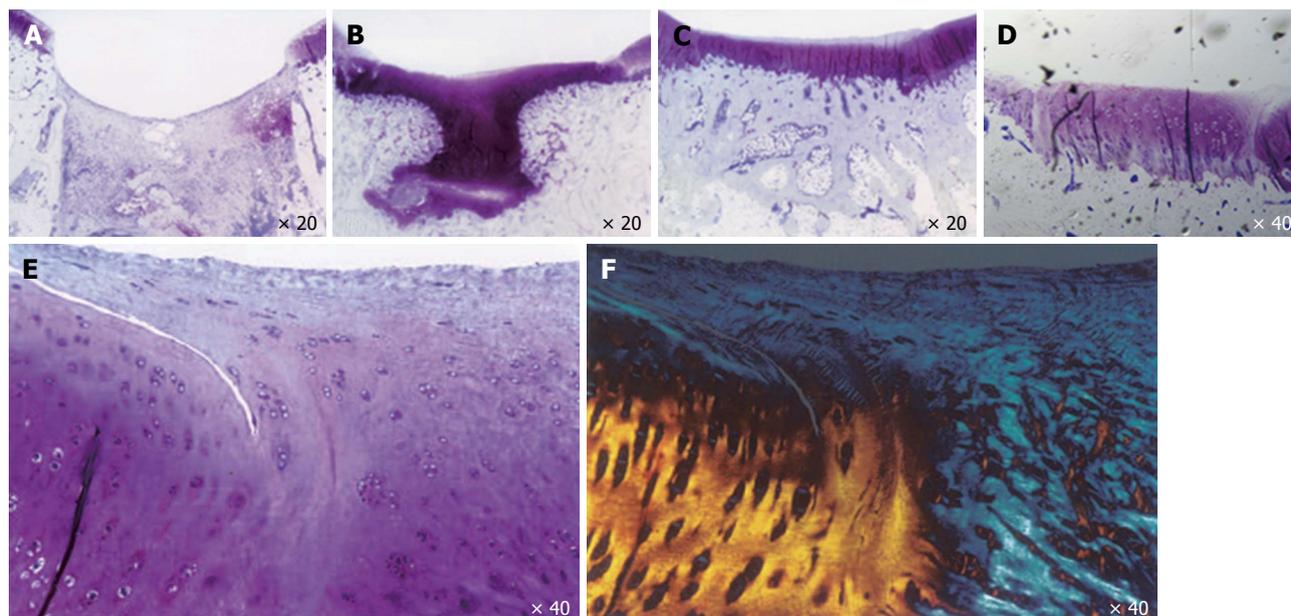


Figure 1 Articular cartilage healing in a microfracture model in adult rabbits. Articular cartilage healing at day 7 (A), 21 (B), 42 (C), and day 84 (D-F). E and F: Lack of healing of reparative cartilage to "normal cartilage" is shown by toluidine blue and polarized light micrographs at day 84.

DEVELOPMENT OF ARTICULAR CHONDROCYTES FROM IPSCS

iPSCs can be derived from a small skin biopsy done with minimal intervention before orthopaedic surgery and can be amplified into virtually limitless amounts of homogeneous cell populations. iPSCs could thus be better than other cell sources to create highly reproducible orthopaedic biologic implants such as for articular cartilage (requiring large amounts of cells). Interestingly, iPSCs apparently produce differentiated cells that exhibit young rather than adult properties, including faster proliferation and creation of healthier, longer-lasting reparative tissues such as the cartilage repair observed in the fetal lamb^[25,36,47-50,52-55].

Recent reports have demonstrated the ability to induce differentiation of iPSCs into different lineages (similar to embryogenesis) by using small molecules, cytokines and overexpression of transgenes^[40,45,56-62]. There are several existing protocols for generating mesenchymal progenitors or MSCs from ESCs and iPSCs that utilize embryoid bodies and/or co-culture with primary cells^[26,29,30,40,46]. These protocols are important steps in developing the use of iPSCs for articular cartilage repair but they have limitations in terms of using either an embryoid body stage or feeder cells which lead to cell heterogeneity or the use of serum which decreases reproducibility.

Two large groups have had a specific interest in chondrogenic differentiation from iPSCs. Tim Hardingham's group has developed techniques using a number of growth factors to differentiate iPSCs to impressive chondrogenic cells with feeder cells and use fibrin as a control group which we believe actually inhibits *in vivo* cartilage repair^[63,64]. Craft *et al*^[65] developed a protocol

with an embryoid body stage with healing in an *in vivo* model with impressive cartilage formation without an adequate control group. Recently, a third group made chondrogenic cells without the use of feeder cells and do not use an embryoid body stage but at the end of their protocol it is not clear why the cells are in suspension, moreover their toluidine blue staining is not similar to that of the adjacent articular cartilage indicating a difference in the sulfated glycosaminoglycans^[30,51,66-69].

CURRENT CHALLENGES IN THE USE OF IPSCS IN ARTICULAR CARTILAGE REPAIR

Chondrogenic differentiation from iPSCs has been demonstrated by monolayer cell culture and in coculture experiments with primary chondrocytes in 3D culture systems such as condensed cell bodies and pellet cultures, but the necessity of coculture conditions increases the chance of contamination of differentiated cells with feeders or other undesired cells^[6,28,70].

A strategy for large-scale production of chondrogenic cells from human ESCs and iPSCs *in vitro* without the use of serum or feeder cells and without the necessity of a condensed cell body step. To aid in the development of an optimal protocol and to avoid the use of feeder cells, serum and the formation of embryoid bodies we plan to use a Quality-by-Design (QbD)-based method similar to that used in the pharmaceutical industry. Specifically the FDA recommends using QbD-based methods to develop new drugs and cell-based treatments for patients^[71]. QbD is a systematic approach that utilizes experimental design and statistical methods in order to gain an in-depth understanding of the effects of input parameters

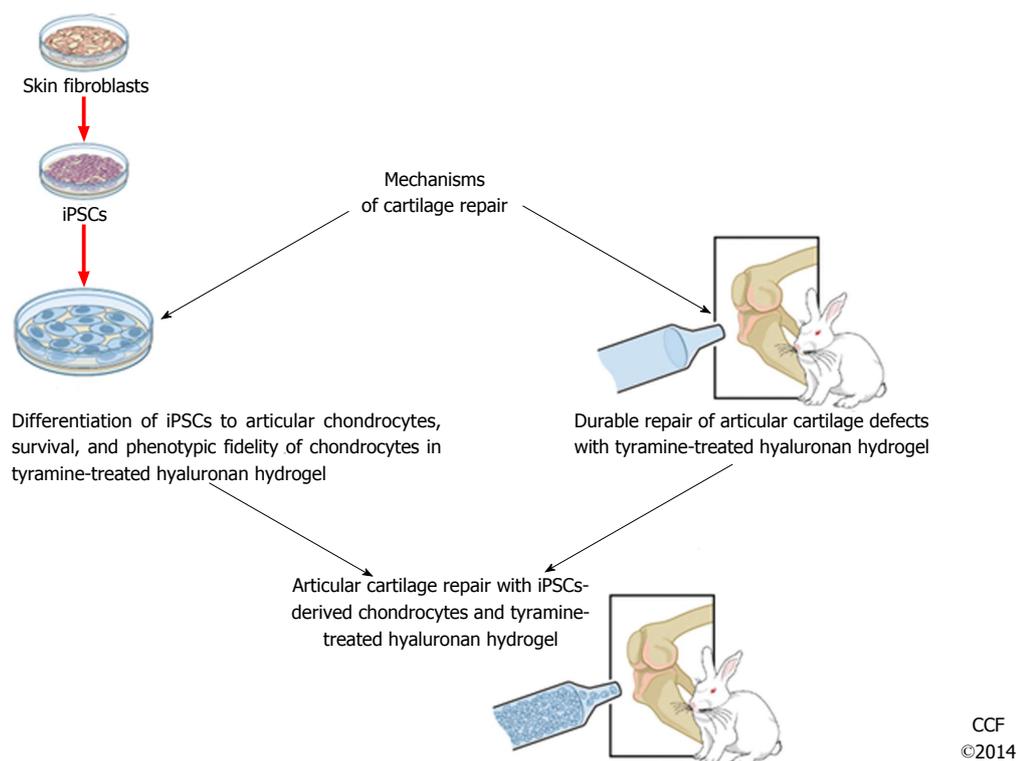


Figure 2 A broad outline for the use of induced pluripotent stem cells in articular cartilage repair. iPSCs: Induced pluripotent stem cells.

and obtain optimal results and quality^[72]. We have begun to apply QbD by implementing the Design-of-Experiment theory and by combining it with Multivariate Data Analysis will more thoroughly and systematically optimize protocols for chondrocyte differentiation from iPSCs.

DISCUSSION

One of the main challenges in using iPSCs for either therapeutic applications or *in vitro* modeling is the difficulty in achieving uniform differentiation of the desired cell type. One cause for a lack of uniform differentiation is the use of serum in the differentiation process of cells, which is imprecise due to batch variability and the presence of undefined extracellular factors within serum. The other primary cause for heterogeneity is the use of feeder cells or an embryoid body stage.

Coculture of MSCs with primary chondrocytes to get chondrogenic differentiation has been used to avoid the inconsistent differentiation of primary MSCs in a cartilage regeneration model^[73-75]. However coculture is problematic as there are contamination issues when the desired cells need to be separated from the feeder cells as mentioned above^[30].

Thus current issues which need to be addressed to further the use of iPSCs in articular cartilage repair and are critically important in cartilage regeneration in an articular cartilage repair model are: (1) Chondrogenic potential and fidelity of the cells; (2) Long term survival of the cells in the repair tissue; (3) Healing to the adjacent endogenous "normal" cartilage in comparison to an adequate untreated control group; and (4) Contamination

with (a) undifferentiated cells that form teratomas with embryoid body formation or (b) with feeder cells used in coculture (Figure 2). Despite these hurdles our group and others have preliminary solutions to these issues. Our group believes that a more systematic approach similar to that used in the pharmaceutical industry could add important information to optimize chondrocyte generation from iPSCs with QbD techniques. We predict that the use of iPSCs clinically for cartilage repair holds the most promise to provide a biologic solution for cartilage damage in the near future and that we and others will be able to optimize protocols applicable for clinical use in cartilage repair in the near future.

REFERENCES

- 1 **Murphy L**, Schwartz TA, Helmick CG, Renner JB, Tudor G, Koch G, Dragomir A, Kalsbeek WD, Luta G, Jordan JM. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum* 2008; **59**: 1207-1213 [PMID: 18759314 DOI: 10.1002/art.24021]
- 2 **Murphy LB**, Helmick CG, Schwartz TA, Renner JB, Tudor G, Koch GG, Dragomir AD, Kalsbeek WD, Luta G, Jordan JM. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. *Osteoarthritis Cartilage* 2010; **18**: 1372-1379 [PMID: 20713163 DOI: 10.1016/j.joca.2010.08.005]
- 3 **Helmick CG**, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, Liang MH, Kremers HM, Mayes MD, Merkel PA, Pillemer SR, Reveille JD, Stone JH. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum* 2008; **58**: 15-25 [PMID: 18163481 DOI: 10.1002/art.23177]
- 4 **Avaliani N**, Sørensen AT, Ledri M, Bengzon J, Koch P, Brüstle O, Deisseroth K, Andersson M, Kokaia M. Optogenetics reveal delayed afferent synaptogenesis on grafted human-induced pluripotent stem cell-derived neural progenitors. *Stem Cells* 2014; **32**:

- 3088-3098 [PMID: 25183299 DOI: 10.1002/stem.1823]
- 5 **Poole AR**, Kobayashi M, Yasuda T, Laverty S, Mwale F, Kojima T, Sakai T, Wahl C, El-Maadawy S, Webb G, Tchetina E, Wu W. Type II collagen degradation and its regulation in articular cartilage in osteoarthritis. *Ann Rheum Dis* 2002; **61** Suppl 2: ii78-ii81 [PMID: 12379630]
 - 6 **Diekman BO**, Christoforou N, Willard VP, Sun H, Sanchez-Adams J, Leong KW, Guilak F. Cartilage tissue engineering using differentiated and purified induced pluripotent stem cells. *Proc Natl Acad Sci USA* 2012; **109**: 19172-19177 [PMID: 23115336 DOI: 10.1073/pnas.1210422109]
 - 7 **Decker RS**, Koyama E, Enomoto-Iwamoto M, Maye P, Rowe D, Zhu S, Schultz PG, Pacifici M. Mouse limb skeletal growth and synovial joint development are coordinately enhanced by Kartogenin. *Dev Biol* 2014; **395**: 255-267 [PMID: 25238962]
 - 8 **Akiyama H**, Kim JE, Nakashima K, Balmes G, Iwai N, Deng JM, Zhang Z, Martin JF, Behringer RR, Nakamura T, de Crombrughe B. Osteo-chondroprogenitor cells are derived from Sox9 expressing precursors. *Proc Natl Acad Sci USA* 2005; **102**: 14665-14670 [PMID: 16203988 DOI: 10.1073/pnas.0504750102]
 - 9 **Koga T**, Matsui Y, Asagiri M, Kodama T, de Crombrughe B, Nakashima K, Takayanagi H. NFAT and Osterix cooperatively regulate bone formation. *Nat Med* 2005; **11**: 880-885 [PMID: 16041384 DOI: 10.1038/nm1270]
 - 10 **Kronenberg HM**. Developmental regulation of the growth plate. *Nature* 2003; **423**: 332-336 [PMID: 12748651 DOI: 10.1038/nature01657]
 - 11 **Benya PD**, Padilla SR, Nimni ME. Independent regulation of collagen types by chondrocytes during the loss of differentiated function in culture. *Cell* 1978; **15**: 1313-1321 [PMID: 729001]
 - 12 **Prockop DJ**. Further proof of the plasticity of adult stem cells and their role in tissue repair. *J Cell Biol* 2003; **160**: 807-809 [PMID: 12642607 DOI: 10.1083/jcb.200302117]
 - 13 **Sekiya I**, Larson BL, Vuoristo JT, Cui JG, Prockop DJ. Adipogenic differentiation of human adult stem cells from bone marrow stroma (MSCs). *J Bone Miner Res* 2004; **19**: 256-264 [PMID: 14969395 DOI: 10.1359/jbmr.0301220]
 - 14 **de Peppo GM**, Vunjak-Novakovic G, Marolt D. Cultivation of human bone-like tissue from pluripotent stem cell-derived osteogenic progenitors in perfusion bioreactors. *Methods Mol Biol* 2014; **1202**: 173-184 [PMID: 24281874 DOI: 10.1007/7651_2013_52]
 - 15 **Bhumiratana S**, Eton RE, Oungoulian SR, Wan LQ, Ateshian GA, Vunjak-Novakovic G. Large, stratified, and mechanically functional human cartilage grown in vitro by mesenchymal condensation. *Proc Natl Acad Sci USA* 2014; **111**: 6940-6945 [PMID: 24778247 DOI: 10.1073/pnas.1324050111]
 - 16 **Ahfeldt T**, Schinzel RT, Lee YK, Hendrickson D, Kaplan A, Lum DH, Camahort R, Xia F, Shay J, Rhee EP, Clish CB, Deo RC, Shen T, Lau FH, Cowley A, Mowrer G, Al-Siddiqi H, Narendorf M, Musunuru K, Gerszten RE, Rinn JL, Cowan CA. Programming human pluripotent stem cells into white and brown adipocytes. *Nat Cell Biol* 2012; **14**: 209-219 [PMID: 22246346 DOI: 10.1038/ncb2411]
 - 17 **Barberi T**, Studer L. Mesenchymal cells. *Methods Enzymol* 2006; **418**: 194-208 [PMID: 17141037 DOI: 10.1016/S0076-6879(06)18012-X]
 - 18 **Baxter MA**, Wynn RF, Jowitt SN, Wraith JE, Fairbairn LJ, Bellantuono I. Study of telomere length reveals rapid aging of human marrow stromal cells following in vitro expansion. *Stem Cells* 2004; **22**: 675-682 [PMID: 15342932 DOI: 10.1634/stemcells.22-5-675]
 - 19 **Sethe S**, Scutt A, Stolzing A. Aging of mesenchymal stem cells. *Ageing Res Rev* 2006; **5**: 91-116 [PMID: 16310414 DOI: 10.1016/j.arr.2005.10.001]
 - 20 **Steinert AF**, Ghivizzani SC, Rethwilm A, Tuan RS, Evans CH, Nöth U. Major biological obstacles for persistent cell-based regeneration of articular cartilage. *Arthritis Res Ther* 2007; **9**: 213 [PMID: 17561986 DOI: 10.1186/ar2195]
 - 21 **Stolzing A**, Jones E, McGonagle D, Scutt A. Age-related changes in human bone marrow-derived mesenchymal stem cells: consequences for cell therapies. *Mech Ageing Dev* 2008; **129**: 163-173 [PMID: 18241911 DOI: 10.1016/j.mad.2007.12.002]
 - 22 **Brittberg M**, Lindahl A, Homminga G, Nilsson A, Isaksson O, Peterson L. A critical analysis of cartilage repair. *Acta Orthop Scand* 1997; **68**: 186-191 [PMID: 9174462]
 - 23 **Brittberg M**, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. *N Engl J Med* 1994; **331**: 889-895 [PMID: 8078550]
 - 24 **Brittberg M**, Nilsson A, Lindahl A, Ohlsson C, Peterson L. Rabbit articular cartilage defects treated with autologous cultured chondrocytes. *Clin Orthop Relat Res* 1996; **(326)**: 270-283 [PMID: 8620653]
 - 25 **Namba RS**, Meuli M, Sullivan KM, Le AX, Adzick NS. Spontaneous repair of superficial defects in articular cartilage in a fetal lamb model. *J Bone Joint Surg Am* 1998; **80**: 4-10 [PMID: 9469302]
 - 26 **Chen YS**, Pelekanos RA, Ellis RL, Horne R, Wolvetang EJ, Fisk NM. Small molecule mesengenic induction of human induced pluripotent stem cells to generate mesenchymal stem/stromal cells. *Stem Cells Transl Med* 2012; **1**: 83-95 [PMID: 23197756 DOI: 10.5966/sctm.2011-0022]
 - 27 **de Peppo GM**, Marcos-Campos I, Kahler DJ, Alsalmán D, Shang L, Vunjak-Novakovic G, Marolt D. Engineering bone tissue substitutes from human induced pluripotent stem cells. *Proc Natl Acad Sci USA* 2013; **110**: 8680-8685 [PMID: 23653480 DOI: 10.1073/pnas.1301190110]
 - 28 **Guzzo RM**, Gibson J, Xu RH, Lee FY, Drissi H. Efficient differentiation of human iPSC-derived mesenchymal stem cells to chondroprogenitor cells. *J Cell Biochem* 2013; **114**: 480-490 [PMID: 22961870 DOI: 10.1002/jcb.24388]
 - 29 **Koyama N**, Miura M, Nakao K, Kondo E, Fujii T, Taura D, Kanamoto N, Sone M, Yasoda A, Arai H, Bessho K, Nakao K. Human induced pluripotent stem cells differentiated into chondrogenic lineage via generation of mesenchymal progenitor cells. *Stem Cells Dev* 2013; **22**: 102-113 [PMID: 22817676 DOI: 10.1089/scd.2012.0127]
 - 30 **Nejadnik H**, Diecke S, Lenkov OD, Chapelin F, Donig J, Tong X, Derugin N, Chan RC, Gaur A, Yang F, Wu JC, Daldrup-Link HE. Improved approach for chondrogenic differentiation of human induced pluripotent stem cells. *Stem Cell Rev* 2015; **11**: 242-253 [PMID: 25578634 DOI: 10.1007/s12015-014-9581-5]
 - 31 **Samuel R**, Daheron L, Liao S, Vardam T, Kamoun WS, Batista A, Buecker C, Schäfer R, Han X, Au P, Scadden DT, Duda DG, Fukumura D, Jain RK. Generation of functionally competent and durable engineered blood vessels from human induced pluripotent stem cells. *Proc Natl Acad Sci USA* 2013; **110**: 12774-12779 [PMID: 23861493 DOI: 10.1073/pnas.1310675110]
 - 32 **Whitworth DJ**, Frith JE, Frith TJ, Ovchinnikov DA, Cooper-White JJ, Wolvetang EJ. Derivation of mesenchymal stromal cells from canine induced pluripotent stem cells by inhibition of the TGF β /activin signaling pathway. *Stem Cells Dev* 2014; **23**: 3021-3033 [PMID: 25055193 DOI: 10.1089/scd.2013.0634]
 - 33 **Carr AJ**, Vugler AA, Hikita ST, Lawrence JM, Gias C, Chen LL, Buchholz DE, Ahmado A, Semo M, Smart MJ, Hasan S, da Cruz L, Johnson LV, Clegg DO, Coffey PJ. Protective effects of human iPSC-derived retinal pigment epithelium cell transplantation in the retinal dystrophic rat. *PLoS One* 2009; **4**: e8152 [PMID: 19997644 DOI: 10.1371/journal.pone.0008152]
 - 34 **Dominici M**, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, Deans R, Keating A, Prockop DJ, Horwitz E. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. *Cytotherapy* 2006; **8**: 315-317 [PMID: 16923606]
 - 35 **Kuroda T**, Yasuda S, Kusakawa S, Hirata N, Kanda Y, Suzuki K, Takahashi M, Nishikawa S, Kawamata S, Sato Y. Highly sensitive in vitro methods for detection of residual undifferentiated cells in retinal pigment epithelial cells derived from human iPSCs. *PLoS One* 2012; **7**: e37342 [PMID: 22615985 DOI: 10.1371/journal.pone.0037342]

- 36 **Takahashi K**, Okita K, Nakagawa M, Yamanaka S. Induction of pluripotent stem cells from fibroblast cultures. *Nat Protoc* 2007; **2**: 3081-3089 [PMID: 18079707 DOI: 10.1038/nprot.2007.418]
- 37 **Koyanagi-Aoi M**, Ohnuki M, Takahashi K, Okita K, Noma H, Sawamura Y, Teramoto I, Narita M, Sato Y, Ichisaka T, Amano N, Watanabe A, Morizane A, Yamada Y, Sato T, Takahashi J, Yamanaka S. Differentiation-defective phenotypes revealed by large-scale analyses of human pluripotent stem cells. *Proc Natl Acad Sci USA* 2013; **110**: 20569-20574 [PMID: 24259714 DOI: 10.1073/pnas.1319061110]
- 38 **Takahashi K**, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 2006; **126**: 663-676 [PMID: 16904174]
- 39 **Inoue H**, Nagata N, Kurokawa H, Yamanaka S. iPSC cells: a game changer for future medicine. *EMBO J* 2014; **33**: 409-417 [PMID: 24500035 DOI: 10.1002/embj.201387098]
- 40 **Taura D**, Noguchi M, Sone M, Hosoda K, Mori E, Okada Y, Takahashi K, Homma K, Oyamada N, Inuzuka M, Sonoyama T, Ebihara K, Tamura N, Itoh H, Suemori H, Nakatsuji N, Okano H, Yamanaka S, Nakao K. Adipogenic differentiation of human induced pluripotent stem cells: comparison with that of human embryonic stem cells. *FEBS Lett* 2009; **583**: 1029-1033 [PMID: 19250937 DOI: 10.1016/j.febslet.2009.02.031]
- 41 **Pagliuca FW**, Millman JR, Gürtler M, Segel M, Van Dervort A, Ryu JH, Peterson QP, Greiner D, Melton DA. Generation of functional human pancreatic β cells in vitro. *Cell* 2014; **159**: 428-439 [PMID: 25303535 DOI: 10.1016/j.cell.2014.09.040]
- 42 **Shiba Y**, Fernandes S, Zhu WZ, Filice D, Muskheili V, Kim J, Palpant NJ, Gantz J, Moyes KW, Reinecke H, Van Biber B, Dardas T, Mignone JL, Izawa A, Hanna R, Viswanathan M, Gold JD, Kotlikoff MI, Sarvazyan N, Kay MW, Murry CE, Laflamme MA. Human ES-cell-derived cardiomyocytes electrically couple and suppress arrhythmias in injured hearts. *Nature* 2012; **489**: 322-325 [PMID: 22864415 DOI: 10.1038/nature11317]
- 43 **Grealish S**, Diguett E, Kirkeby A, Mattsson B, Heuer A, Bramouille Y, Van Camp N, Perrier AL, Hantraye P, Björklund A, Parmar M. Human ESC-derived dopamine neurons show similar preclinical efficacy and potency to fetal neurons when grafted in a rat model of Parkinson's disease. *Cell Stem Cell* 2014; **15**: 653-665 [PMID: 25517469 DOI: 10.1016/j.stem.2014.09.017]
- 44 **Schwartz SD**, Regillo CD, Lam BL, Elliott D, Rosenfeld PJ, Gregori NZ, Hubschman JP, Davis JL, Heilwell G, Spirn M, Maguire J, Gay R, Bateman J, Ostrick RM, Morris D, Vincent M, Anglade E, Del Priore LV, Lanza R. Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase 1/2 studies. *Lancet* 2015; **385**: 509-516 [PMID: 25458728 DOI: 10.1016/S0140-6736(14)61376-3]
- 45 **Inui A**, Iwakura T, Reddi AH. Human stem cells and articular cartilage regeneration. *Cells* 2012; **1**: 994-1009 [PMID: 24710539 DOI: 10.3390/cells1040994]
- 46 **Gong G**, Ferrari D, Dealy CN, Kosher RA. Direct and progressive differentiation of human embryonic stem cells into the chondrogenic lineage. *J Cell Physiol* 2010; **224**: 664-671 [PMID: 20432462 DOI: 10.1002/jcp.22166]
- 47 **Maherali N**, Sridharan R, Xie W, Utikal J, Eminli S, Arnold K, Stadtfeld M, Yachechko R, Tchieu J, Jaenisch R, Plath K, Hochedlinger K. Directly reprogrammed fibroblasts show global epigenetic remodeling and widespread tissue contribution. *Cell Stem Cell* 2007; **1**: 55-70 [PMID: 18371336]
- 48 **Meissner A**, Wernig M, Jaenisch R. Direct reprogramming of genetically unmodified fibroblasts into pluripotent stem cells. *Nat Biotechnol* 2007; **25**: 1177-1181 [PMID: 17724450]
- 49 **Sommer AG**, Rozelle SS, Sullivan S, Mills JA, Park SM, Smith BW, Iyer AM, French DL, Kotton DN, Gadue P, Murphy GJ, Mostoslavsky G. Generation of human induced pluripotent stem cells from peripheral blood using the STEMCCA lentiviral vector. *J Vis Exp* 2012; pii: 4327 [PMID: 23149977 DOI: 10.3791/4327]
- 50 **Yamanaka S**, Li J, Kania G, Elliott S, Wersto RP, Van Eyk J, Wobus AM, Boheler KR. Pluripotency of embryonic stem cells. *Cell Tissue Res* 2008; **331**: 5-22 [PMID: 18026755]
- 51 **Yamashita A**, Morioka M, Yahara Y, Okada M, Kobayashi T, Kuriyama S, Matsuda S, Tsumaki N. Generation of scaffoldless hyaline cartilaginous tissue from human iPSCs. *Stem Cell Reports* 2015; **4**: 404-418 [PMID: 25733017 DOI: 10.1016/j.stemcr.2015.01.016]
- 52 **Buganim Y**, Markoulaki S, van Wietmarschen N, Hoke H, Wu T, Ganz K, Akhtar-Zaidi B, He Y, Abraham BJ, Porubsky D, Kulenkampff E, Faddah DA, Shi L, Gao Q, Sarkar S, Cohen M, Goldmann J, Nery JR, Schultz MD, Ecker JR, Xiao A, Young RA, Lansdorp PM, Jaenisch R. The developmental potential of iPSCs is greatly influenced by reprogramming factor selection. *Cell Stem Cell* 2014; **15**: 295-309 [PMID: 25192464 DOI: 10.1016/j.stem.2014.07.003]
- 53 **Chen G**, Gulbranson DR, Hou Z, Bolin JM, Ruotti V, Probasco MD, Smuga-Otto K, Howden SE, Diol NR, Propson NE, Wagner R, Lee GO, Antosiewicz-Bourget J, Teng JM, Thomson JA. Chemically defined conditions for human iPSC derivation and culture. *Nat Methods* 2011; **8**: 424-429 [PMID: 21478862 DOI: 10.1038/nmeth.1593]
- 54 **Hockemeyer D**, Wang H, Kiani S, Lai CS, Gao Q, Cassady JP, Cost GJ, Zhang L, Santiago Y, Miller JC, Zeitler B, Cheron JM, Meng X, Hinkley SJ, Rebar EJ, Gregory PD, Urnov FD, Jaenisch R. Genetic engineering of human pluripotent cells using TALE nucleases. *Nat Biotechnol* 2011; **29**: 731-734 [PMID: 21738127 DOI: 10.1038/nbt.1927]
- 55 **Soldner F**, Laganière J, Cheng AW, Hockemeyer D, Gao Q, Alagappan R, Khurana V, Golbe LI, Myers RH, Lindquist S, Zhang L, Guschin D, Fong LK, Vu BJ, Meng X, Urnov FD, Rebar EJ, Gregory PD, Zhang HS, Jaenisch R. Generation of isogenic pluripotent stem cells differing exclusively at two early onset Parkinson point mutations. *Cell* 2011; **146**: 318-331 [PMID: 21757228 DOI: 10.1016/j.cell.2011.06.019]
- 56 **Alfred R**, Taiani JT, Krawetz RJ, Yamashita A, Rancourt DE, Kallos MS. Large-scale production of murine embryonic stem cell-derived osteoblasts and chondrocytes on microcarriers in serum-free media. *Biomaterials* 2011; **32**: 6006-6016 [PMID: 21620471 DOI: 10.1016/j.biomaterials.2011.04.015]
- 57 **Noguchi M**, Hosoda K, Nakane M, Mori E, Nakao K, Taura D, Yamamoto Y, Kusakabe T, Sone M, Sakurai H, Fujikura J, Ebihara K, Nakao K. In vitro characterization and engraftment of adipocytes derived from human induced pluripotent stem cells and embryonic stem cells. *Stem Cells Dev* 2013; **22**: 2895-2905 [PMID: 23750558 DOI: 10.1089/scd.2013.0113]
- 58 **Guzzo RM**, Scanlon V, Sanjay A, Xu RH, Drissi H. Establishment of human cell type-specific iPSCs with enhanced chondrogenic potential. *Stem Cell Rev* 2014; **10**: 820-829 [PMID: 24958240 DOI: 10.1007/s12015-014-9538-8]
- 59 **Okada M**, Ikegawa S, Morioka M, Yamashita A, Saito A, Sawai H, Murotsuki J, Ohashi H, Okamoto T, Nishimura G, Imaizumi K, Tsumaki N. Modeling type II collagenopathy skeletal dysplasia by directed conversion and induced pluripotent stem cells. *Hum Mol Genet* 2015; **24**: 299-313 [PMID: 25187577 DOI: 10.1093/hmg/ddu444]
- 60 **Outani H**, Okada M, Yamashita A, Nakagawa K, Yoshikawa H, Tsumaki N. Direct induction of chondrogenic cells from human dermal fibroblast culture by defined factors. *PLoS One* 2013; **8**: e77365 [PMID: 24146984 DOI: 10.1371/journal.pone.0077365]
- 61 **Tsumaki N**, Okada M, Yamashita A. iPSC cell technologies and cartilage regeneration. *Bone* 2015; **70**: 48-54 [PMID: 25026496 DOI: 10.1016/j.bone.2014.07.011]
- 62 **Uto S**, Nishizawa S, Takasawa Y, Asawa Y, Fujihara Y, Takato T, Hoshi K. Bone and cartilage repair by transplantation of induced pluripotent stem cells in murine joint defect model. *Biomed Res* 2013; **34**: 281-288 [PMID: 24389404]
- 63 **Cheng A**, Kapacee Z, Peng J, Lu S, Lucas RJ, Hardingham TE, Kimber SJ. Cartilage repair using human embryonic stem cell-derived chondroprogenitors. *Stem Cells Transl Med* 2014; **3**: 1287-1294 [PMID: 25273540 DOI: 10.5966/sctm.2014-0101]
- 64 **Oldershaw RA**, Baxter MA, Lowe ET, Bates N, Grady LM,

- Soncin F, Brison DR, Hardingham TE, Kimber SJ. Directed differentiation of human embryonic stem cells toward chondrocytes. *Nat Biotechnol* 2010; **28**: 1187-1194 [PMID: 20967028 DOI: 10.1038/nbt.1683]
- 65 **Craft AM**, Rockel JS, Nartiss Y, Kandel RA, Alman BA, Keller GM. Generation of articular chondrocytes from human pluripotent stem cells. *Nat Biotechnol* 2015; **33**: 638-645 [PMID: 25961409 DOI: 10.1038/nbt.3210]
- 66 **Mobasheri A**, Csaki C, Clutterbuck AL, Rahmanzadeh M, Shakibaei M. Mesenchymal stem cells in connective tissue engineering and regenerative medicine: applications in cartilage repair and osteoarthritis therapy. *Histol Histopathol* 2009; **24**: 347-366 [PMID: 19130405]
- 67 **Mobasheri A**, Kalamegam G, Musumeci G, Batt ME. Chondrocyte and mesenchymal stem cell-based therapies for cartilage repair in osteoarthritis and related orthopaedic conditions. *Maturitas* 2014; **78**: 188-198 [PMID: 24855933 DOI: 10.1016/j.maturitas.2014.04.017]
- 68 **Guilak F**, Estes BT, Diekman BO, Moutos FT, Gimble JM. 2010 Nicolas Andry Award: Multipotent adult stem cells from adipose tissue for musculoskeletal tissue engineering. *Clin Orthop Relat Res* 2010; **468**: 2530-2540 [PMID: 20625952 DOI: 10.1007/s11999-010-1410-9]
- 69 **Cheng A**, Hardingham TE, Kimber SJ. Generating cartilage repair from pluripotent stem cells. *Tissue Eng Part B Rev* 2014; **20**: 257-266 [PMID: 23957872 DOI: 10.1089/ten.TEB.2012.0757]
- 70 **Craft AM**, Ahmed N, Rockel JS, Baht GS, Alman BA, Kandel RA, Grigoriadis AE, Keller GM. Specification of chondrocytes and cartilage tissues from embryonic stem cells. *Development* 2013; **140**: 2597-2610 [PMID: 23715552 DOI: 10.1242/dev.087890]
- 71 **Schachter B**. Therapies of the state. *Nat Biotechnol* 2014; **32**: 736-741 [PMID: 25093881 DOI: 10.1038/nbt.2984]
- 72 **Mercier SM**, Diepenbroek B, Wijffels RH, Streefland M. Multi-variate PAT solutions for biopharmaceutical cultivation: current progress and limitations. *Trends Biotechnol* 2014; **32**: 329-336 [PMID: 24732022 DOI: 10.1016/j.tibtech.2014.03.008]
- 73 **Lai JH**, Kajiyama G, Smith RL, Maloney W, Yang F. Stem cells catalyze cartilage formation by neonatal articular chondrocytes in 3D biomimetic hydrogels. *Sci Rep* 2013; **3**: 3553 [PMID: 24352100 DOI: 10.1038/srep03553]
- 74 **Qu C**, Puttonen KA, Lindeberg H, Ruponen M, Hovatta O, Koistinaho J, Lammi MJ. Chondrogenic differentiation of human pluripotent stem cells in chondrocyte co-culture. *Int J Biochem Cell Biol* 2013; **45**: 1802-1812 [PMID: 23735325 DOI: 10.1016/j.biocel.2013.05.029]
- 75 **Bigdeli N**, Karlsson C, Strehl R, Concaro S, Hyllner J, Lindahl A. Coculture of human embryonic stem cells and human articular chondrocytes results in significantly altered phenotype and improved chondrogenic differentiation. *Stem Cells* 2009; **27**: 1812-1821 [PMID: 19544424 DOI: 10.1002/stem.114]

P- Reviewer: Danisovic L, Musumeci G
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Evidence base and future research directions in the management of low back pain

Allan Abbott

Allan Abbott, Department of Medical and Health Sciences, Division of Physiotherapy, Faculty of Health Sciences, Linköping University, SE 58183 Linköping, Sweden

Allan Abbott, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229, Australia

Author contributions: Abbott A contributed solely to this editorial.

Conflict-of-interest statement: The author has no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Allan Abbott, PhD, Med Dr, MSc Physio, Grad Cert Clin Ed, BExSci, Department of Medical and Health Sciences, Division of Physiotherapy, Faculty of Health Sciences, Linköping University, Lasarettsgatan, SE 58183 Linköping, Sweden. allan.abbott@liu.se
 Telephone: +46-13-282495
 Fax: +46-13-145004

Received: September 18, 2015
 Peer-review started: September 22, 2015
 First decision: October 30, 2015
 Revised: November 17, 2015
 Accepted: December 18, 2015
 Article in press: December 21, 2015
 Published online: March 18, 2016

Abstract

Low back pain (LBP) is a prevalent and costly condition. Awareness of valid and reliable patient history taking,

physical examination and clinical testing is important for diagnostic accuracy. Stratified care which targets treatment to patient subgroups based on key characteristics is reliant upon accurate diagnostics. Models of stratified care that can potentially improve treatment effects include prognostic risk profiling for persistent LBP, likely response to specific treatment based on clinical prediction models or suspected underlying causal mechanisms. The focus of this editorial is to highlight current research status and future directions for LBP diagnostics and stratified care.

Key words: Low back pain; Diagnostics; Prognostics; Stratification; Treatment

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Knowledge of the current research status and future directions for low back pain diagnostics and stratified care is essential to help engage clinicians in evidence based practice and to potentially improve patient management.

Abbott A. Evidence base and future research directions in the management of low back pain. *World J Orthop* 2016; 7(3): 156-161 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/156.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.156>

INTRODUCTION

Low back pain (LBP) is a prevalent and burdensome problem for individuals and society worldwide^[1,2]. LBP is often defined in terms of its localization, duration, severity, frequency, and interference on activities of daily living^[3]. Most episodes of LBP are self-limiting but approximately 20% develop chronic symptoms^[1]. The etiology of LBP is often classified as specific or non-

specific, based upon if a pathoanatomical cause can be identified through objective diagnostic assessment and confirmed by medical imaging^[4]. The prevalence of LBP caused by specific pathology of serious nature such as malignancy, spinal fracture, infection, or cauda equine syndrome requiring secondary or tertiary health care has been reported to range between < 1%-4% in the primary health care setting^[5,6]. Furthermore, nerve root problems associated with radiculopathy or spinal stenosis are thought to explain approximately 5%-15% of cases^[7,8]. Medical imaging studies have highlighted that approximately 50% of younger adults and 90% of older adults have degenerative findings and large variations in lumbar spine morphology^[9]. This is however evident in both symptomatic and asymptomatic individuals which renders diagnosis of specific LBP prone to false-positive results. The choice of treatment merely based on benign anatomic impairment or individual clinical assessment techniques with low diagnostic accuracy is controversial and may result in suboptimal outcomes^[10]. Treatment focused on patient specific and modifiable pain mechanisms assessed with accurate diagnostics has the potential to improve patient outcomes. Therefore, research in these topics is of utmost importance.

EVIDENCE BASE FOR THE ASSESSMENT OF LBP AND FUTURE RESEARCH DIRECTIONS

Guidelines published nationally and internationally recommend diagnostic triage (non-specific LBP, radicular syndrome, serious pathology), screening for serious pathology using red flags, screening of psychosocial risk factors, physical examination for neurologic screening, and the avoidance of routine imaging for non-specific LBP^[11].

Valid and reliable assessment procedures are required to accurately understand the clinical presentation of pain. Recent Cochrane diagnostic test accuracy reviews have reported that the many red flags reported in clinical guidelines display low individual diagnostic accuracy^[5,6]. However, a combination of red flags such as significant trauma, older age, corticosteroid use and the presence of contusion improve the diagnostic accuracy of vertebral fractures^[5]. For the identification of spinal cancer, a history of cancer was the only useful red flag meaningfully increasing the likelihood of cancer^[6]. Raison *et al*^[12] reported that bowel and bladder dysfunction and saddle sensory disturbance where significant red flags but only marginally raise clinical suspicion of spinal cord or cauda equina compression.

A systematic review of literature by Shultz *et al*^[13] displayed how history items such as age > 50, lower extremity pain or numbness, symptoms relieved with sitting/bending over and symptoms exacerbated with standing/walking suggests lumbar spinal stenosis in patients with LBP and non-specific lower extremity symptoms. Furthermore, a limited amount of literature for the diagnosis of nerve root compression/radiculopathy

suggests that, dermatomal distribution/radiation was the history component with the largest diagnostic odds ratio followed by history of nerve injury, more pain on coughing, sneezing or straining, leg pain, subjective muscle weakness, subjective sensory loss, and disturbed urinary passage^[13]. Regarding the diagnosis of lumbar disc herniation, a limited amount of literature suggests previous non-spinal surgery, education level and progressive sciatic pain to be significant history components^[13]. Kasai *et al*^[14] reported symptoms exacerbated by specific movements such as standing up and rolling over and the timing of symptoms such as morning pain could assist clinicians in diagnosing structural lumbar segmental instability. When no anatomical abnormality is suggested in the patient's history, patients with pain or aggravating/easing factors disproportionate to injury, along with psychosocial symptoms were very likely to be diagnosed with central sensitization. Similarly, patients with localized or intermittent pain were more likely to be diagnosed with nociceptive LBP^[13]. The future research direction for the value of patient history will focus on clustering items to improve diagnostic accuracy.

The physical examination aims to confirm or rule out serious pathological condition or neurological compromise and classify body function impairments and activity limitations. Systematic literature reviews suggest that neurological examination including muscle weakness, muscle wasting, impaired reflexes and sensory deficits display poor pooled diagnostic accuracy values with low individual sensitivity and moderate specificity for surgically and radiologically confirmed disc herniation and the identification of affected segmental level^[15,16]. Mechanical diagnostic tests such as forward flexion, hyper-extension test, and slump test have slightly better diagnostic accuracy and combining positive test results increased the specificity of physical tests^[15]. The straight leg raising (SLR) test has high sensitivity and widely varying specificity while the crossed SLR showed high specificity with low sensitivity^[15].

A systematic review by Hancock *et al*^[17] reported that high intensity zone, endplate changes and disc degeneration assessed on magnetic resonance imaging are informative for the disc being the source of LBP. The only clinical feature found to increase the likelihood of the disc as the source of pain was the centralization phenomena. Manual tests of the sacroiliac joint when use in combination were informative but none of the tests for facet joint pain were found to be informative to distinguish the source of LBP. A systematic review by Alqarni *et al*^[18] showed that high specificity and moderate to high sensitivity for lumbar spinous process palpation test for the diagnostic test for lumbar spondylolisthesis. Another systematic review by Alqarni *et al*^[19] showed the passive lumbar extension test may be useful in orthopaedic clinical practice to diagnose structural lumbar segmental instability.

Studies investigating the reliability of mechanical LBP provocation test show varying results and methodological qualities. Low reliability is often reported in palpation-based assessment but improves to moderate reliability

when based on symptom response^[20]. Furthermore, timed muscle endurance tests and symptom response with repeated movements have high reliability^[20]. The reliability of the SLR procedures are considered good in most studies^[21]. Carlsson and Rasmussen-Barr^[22] in a systematic review of reliability of functional and active movement control tests to identify movement dysfunction in LBP showed that prone knee bend and one leg stance have moderate and good reliability across studies with low risk of bias.

Future research directions recommended in the literature focus on the clustering of diagnostic tests to improve the diagnostic accuracy for identifying specific diagnostic subgroups. This research direction is closely aligned with the process of clinical decision making^[23].

EVIDENCE BASE FOR PRIMARY HEALTH CARE INTERVENTIONS FOR LBP AND FUTURE RESEARCH DIRECTIONS

Therapeutic recommendations from guidelines published nationally and internationally discourage the use of bed rest and therapeutic ultrasound as well as the solitary use of electrotherapy^[11]. Early and gradual return to normal functioning and activities, the time-contingent use of paracetamol progressing to non-steroidal anti-inflammatories, and the assessment of psychosocial risk factors for chronicity are recommended^[11] based on a low number of randomized controlled trials (RCTs) with overall low methodological quality showing significant analgesic and/or functional effects^[24-27]. As LBP persists, the guidelines recommend therapies such as supervised exercise, manual therapy, acupuncture, cognitive behavioral therapy and multidisciplinary treatments^[11] based on a low number of RCTs with overall low-moderate methodological quality showing significant analgesic and/or functional effects^[24-27].

Research investigating the effectiveness of conservative interventions for LBP have often reported small to moderate effect sizes in the short term with no longer-term effect on LBP trajectories for patients^[24-27]. These studies may however be confounded due to heterogeneous pooling of patients and treatment modalities where average treatment effect masks patient's responding with large effect or little or no effect^[28]. This has led to an increased research focus on stratified care which targets treatment to patient subgroups based on key characteristics such as their prognostic risk profile for persistent LBP, likely response to specific treatment based on clinical prediction models (CPRs) or suspected underlying causal mechanisms^[29].

The STarT Back approach stratifies patients based on a multi-domain prognostic model to determine patients at low, medium and high risk of persistent back pain. Patients at medium and high risk are referred for more extensive treatment while those at low risk can be reassured and offered minimal treatment. The model performed well in a validation study and impact analysis

and is current undergoing broader external validation^[29].

Another option is to take aspects of the patient history, physical examination and clinical test findings to match the patient to treatment based on the prediction of responsiveness to a specific treatment. Currently 13 CPRs for LBP have been developed from clustering of diagnostic clinical tests^[30]. Most of these CPR for LBP are in their initial development phase with only 1 tool for identifying lumbar spinal stenosis and 2 tools for identifying inflammatory back pain having undergone validation and no studies have yet undergone impact analysis^[30]. Furthermore 30 prognostic LBP CPRs have been developed with 3 having undergone validation including the Cassandra rule for predicting long-term significant functional limitations and the five-item and two-item Flynn manipulation CPRs for predicting a favorable functional prognosis in patients being treated with lumbopelvic manipulation^[31].

Targeted treatment can also be based on underlying mechanisms of the patient's LBP. For example, mechanism-based classifications of pain aim to define if underlying nociceptive, neuropathic, central sensitization, autonomic/motor, or affective neurophysiological mechanisms are driving the LBP^[4]. Other classifications include the Pathoanatomic Based Classification approach and the Mechanical Diagnosis and Treatment approach. These models have nonetheless been criticized for aspects of poor validity and reliability, not covering all dimensions of the biopsychosocial nature of LBP and not adequately being tested in RCTs^[29,32]. The Classification based Cognitive Functional Therapy approach integrates pathoanatomical, neurophysiological, psychosocial, physical and lifestyle domains. It has been validated in a RCT but has not undergone impact analysis or broader external validation^[33]. The approach requires effective communication, education of body relaxation strategies, the normalization of functional movement patterns and discouragement of pain behaviors and utilization of mindfulness and motivational principles^[29].

Fersum *et al*^[32] reported in their systematic review and meta-analysis that a statistical significant difference exists in favor of the classification-based intervention for reductions in LBP and disability in the short and long-term with moderate effect size reported in the short term. However, only 7.4% of published RCT studies had performed sub-classification beyond applying general inclusion and exclusion criteria and matched interventions^[32]. Fairbank *et al*^[34] suggested that future efforts in developing classification systems should focus on one that helps to direct both surgical and nonsurgical treatments.

EVIDENCE BASE FOR SECONDARY/ TERTIARY HEALTH CARE INTERVENTIONS FOR LBP AND FUTURE RESEARCH DIRECTIONS

While primary health care is the first step in the mana-

gement of LBP, in the case of persistent pain despite primary health care intervention and in the presence of a clear pathoanatomic pain mechanism, secondary health care in the form of surgical intervention may be indicated. With regards to isthmic spondylolisthesis, one study with a high risk of bias has indicated that surgery leads to better improvement in pain and overall clinical outcome compared to conservative treatment, while the different surgical techniques show conflicting results^[35]. Regarding degenerative spondylolisthesis, fusion results in better clinical outcomes than decompression, but there is a lack of evidence regarding if instrumented or non-instrumented fusion is optimal and there is a need for comparisons with conservative treatment^[36]. For spinal stenosis, there are heterogeneous studies of low methodological quality suggesting that surgery result in better leg pain and disability outcomes compared conservative treatment^[37]. Considering that the prevalence of lumbar spinal stenosis with neurogenic claudication is expected to rise with an aging population, large high-quality trials comparing surgery and conservative treatment are warranted^[37].

A recent systematic review and meta-analysis suggests that there is strong evidence that lumbar fusion surgery is not more effective than conservative treatment in reducing disability because of chronic LBP^[38]. In a review of systematic reviews and RCTs, Jacobs *et al*^[36] reported that for discogenic LBP, surgery is no more effective than high-intensity conservative interventions for improvements in pain scores or function. Similarly disc replacement results in equal success rates as surgical fusion does^[36]. With regards to disc herniation with radiculopathy, surgery leads to short-term benefits for leg pain and to a lesser extent for LBP. Despite this, no short-term and long term effects have been observed for functional outcomes measures. Furthermore, the different surgical techniques show no differences in outcomes. There is currently a lack of high quality RCTs comparing conservative or surgical treatment for disc herniation with or without sciatica^[36].

There are differing views about how a patient should prepare for and afterwards undergo rehabilitation for lumbar spinal surgery. The evidence base is evolving as are the differing opinions. In the past, surgeons have commonly restricted the amount of active rehabilitation after surgery in the belief that it may prevent complications during healing. Usual care has therefore often consisted of limited advice to stay active postoperatively and has sometimes included brief general exercise programs. It has however become more apparent the importance to optimizing pre- and post-operative care in aid to improve patient outcomes.

A recent systematic review and meta-analysis by Oosterhuis *et al*^[39] summarized 22 clinical trials investigating the effectiveness of rehabilitation after first-time lumbar discectomy surgery. The results suggest that exercise programs conducted four to six weeks post-operatively result in less pain and disability with small to medium effect sizes compared to usual care.

Furthermore, rapid reduction in pain and disability occurred in high intensity exercise programs compared to low intensity programs. Supervised or home exercise programs did not show significant differences for pain relief or disability. There were no indications that re-operation rate increased as a result of active rehabilitation programs after first-time lumbar disc surgery^[39]. The study's active rehabilitation programs consisted of exercise therapy, strength and mobility training, physiotherapy and multidisciplinary programs. More specifically, these included back schools, ergonomics education, motor control modification, resumption of activities of daily living including work and physical activity and enhancement of pain coping strategies delivered by individual sessions, group training or education or a combination of these. The quality of evidence was concluded to be low as more than half of the studies had high risk of bias and heterogeneity in rehabilitation programs warranting the need for more research with methodological rigor and the stratification of rehabilitation content^[39]. Findings from a recently published RCTs from Ozkara *et al*^[40] support the conclusion drawn by Oosterhuis *et al*^[39]. Furthermore in a RCT conducted by Louw *et al*^[41], preoperative neuroscience education for lumbar radiculopathy resulted in significantly better patient-rated preparation for lumbar discectomy surgery, fulfillment of postoperative expectations as well as less health care utilization compared to usual preoperative education provided by surgeons and staff.

Another systematic review and meta-analysis has investigated the effectiveness of rehabilitation after spinal stenosis surgery from 3 existing RCTs^[42]. The study's active rehabilitation programs focused on functional outcomes and used group or therapist-led exercise or educational materials encouraging activity starting between 6 and 12 wk after surgery. The review highlighted that active rehabilitation is more effective than usual care for improving functional status and LBP both in the short and long-term. Furthermore long term improvements were seen for the reduction of leg pain. The review as a whole concluded that despite the studies having low risk of bias, the small number of relevant studies rendered the quality of evidence as very low. Additional research including stratification of rehabilitation content is warranted^[42].

With regards to rehabilitation after lumbar spinal fusion, several RCT's have highlighted that the integration of active rehabilitation and cognitive behavioral programs improve patient functional and pain outcomes significantly more than usual care^[43-45]. Nielsen *et al*^[46] conducted an RCT taking a structured pre-habilitation and early rehabilitation program compared to standard care. The structured pre-habilitation and early rehabilitation program consisted of muscle strengthening exercise for the back and abdomen as well as cardiovascular conditioning, analgesics and a nutritional program. The integrated program of pre-habilitation and early rehabilitation improved the outcome and shortened

the hospital stay, without more complications, pain or dissatisfaction. Only one existing study has reported prospective outcomes of a structured rehabilitation program after total disc replacement (TDR). Canbulat *et al*^[47] reported good outcomes with regards to early pain relief and return to activities when combining careful patient selection, surgical technique, and a structured rehabilitation program. Furthermore, a large retrospective study has highlighted that 4 or more sessions of clinic-based physiotherapy produces better functional disability, pain and quality of life outcomes compared with self-mediated rehabilitation after TDR^[48]. In conclusion, more research is need using a stratified biopsychosocial approach to pre-habilitation and rehabilitation of patients undergoing lumbar spine surgery.

REFERENCES

- Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, Woolf A, Vos T, Buchbinder R. A systematic review of the global prevalence of low back pain. *Arthritis Rheum* 2012; **64**: 2028-2037 [PMID: 22231424 DOI: 10.1002/art.34347]
- Hoy D, March L, Brooks P, Blyth F, Woolf A, Bain C, Williams G, Smith E, Vos T, Barendregt J, Murray C, Burstein R, Buchbinder R. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; **73**: 968-974 [PMID: 24665116 DOI: 10.1136/annrheumdis-2013-204428]
- Dionne CE, Dunn KM, Croft PR, Nachemson AL, Buchbinder R, Walker BF, Wyatt M, Cassidy JD, Rossignol M, Leboeuf-Yde C, Hartvigsen J, Leino-Arjas P, Latza U, Reis S, Gil Del Real MT, Kovacs FM, Oberg B, Cedraschi C, Bouter LM, Koes BW, Picavet HS, van Tulder MW, Burton K, Foster NE, Macfarlane GJ, Thomas E, Underwood M, Waddell G, Shekelle P, Volinn E, Von Korf M. A consensus approach toward the standardization of back pain definitions for use in prevalence studies. *Spine (Phila Pa 1976)* 2008; **33**: 95-103 [PMID: 18165754 DOI: 10.1097/BRS.0b013e31815e7f94]
- Smart KM, O'Connell NE, Doody C. Towards a mechanisms-based classification of pain in musculoskeletal physiotherapy? *Phys Ther Rev* 2008; **13**: 1-10 [DOI: 10.1179/174328808X251984]
- Williams CM, Henschke N, Maher CG, van Tulder MW, Koes BW, Macaskill P, Irwig L. Red flags to screen for vertebral fracture in patients presenting with low-back pain. *Cochrane Database Syst Rev* 2013; **1**: CD008643 [PMID: 23440831 DOI: 10.1002/14651858.CD008643.pub2]
- Henschke N, Maher CG, Ostelo RW, de Vet HC, Macaskill P, Irwig L. Red flags to screen for malignancy in patients with low-back pain. *Cochrane Database Syst Rev* 2013; **2**: CD008686 [PMID: 23450586 DOI: 10.1002/14651858.CD008686.pub2]
- Konstantinou K, Dunn KM. Sciatica: review of epidemiological studies and prevalence estimates. *Spine (Phila Pa 1976)* 2008; **33**: 2464-2472 [PMID: 18923325 DOI: 10.1097/BRS.0b013e318183a4a2]
- Yabuki S, Fukumori N, Takegami M, Onishi Y, Otani K, Sekiguchi M, Wakita T, Kikuchi S, Fukuhara S, Konno S. Prevalence of lumbar spinal stenosis, using the diagnostic support tool, and correlated factors in Japan: a population-based study. *J Orthop Sci* 2013; **18**: 893-900 [PMID: 23963588 DOI: 10.1007/s00776-013-0455-5]
- Brinjikji W, Luetmer PH, Comstock B, Bresnahan BW, Chen LE, Deyo RA, Halabi S, Turner JA, Avins AL, James K, Wald JT, Kallmes DF, Jarvik JG. Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. *AJNR Am J Neuroradiol* 2015; **36**: 811-816 [PMID: 25430861 DOI: 10.3174/ajnr.A4173]
- Endean A, Palmer KT, Coggon D. Potential of magnetic resonance imaging findings to refine case definition for mechanical low back pain in epidemiological studies: a systematic review. *Spine (Phila Pa 1976)* 2011; **36**: 160-169 [PMID: 20739918 DOI: 10.1097/BRS.0b013e3181cd9adb]
- Koes BW, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J* 2010; **19**: 2075-2094 [PMID: 20602122 DOI: 10.1007/s00586-010-1502-y]
- Raison NT, Alwan W, Abbot A, Farook M, Khaleel A. The reliability of red flags in spinal cord compression. *Arch Trauma Res* 2014; **3**: e17850 [PMID: 25032171 DOI: 10.5812/atr.17850]
- Shultz S, Averell K, Eickelman A, Sanker H, Donaldson MB. Diagnostic accuracy of self-report and subjective history in the diagnosis of low back pain with non-specific lower extremity symptoms: A systematic review. *Man Ther* 2015; **20**: 18-27 [PMID: 25231775 DOI: 10.1016/j.math.2014.08.002]
- Kasai Y, Morishita K, Takegami K, Uchida A. Clinical symptoms of patients with lumbar spinal instability. *Clin Orthop Surg* 2003; **38**: 463-467
- van der Windt DA, Simons E, Riphagen II, Ammendolia C, Verhagen AP, Laslett M, Devillé W, Deyo RA, Bouter LM, de Vet HC, Aertgeerts B. Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain. *Cochrane Database Syst Rev* 2010; **2**: CD007431 [PMID: 20166095 DOI: 10.1002/14651858.CD007431.pub2]
- Al Nezari NH, Schneiders AG, Hendrick PA. Neurological examination of the peripheral nervous system to diagnose lumbar spinal disc herniation with suspected radiculopathy: a systematic review and meta-analysis. *Spine J* 2013; **13**: 657-674 [PMID: 23499340 DOI: 10.1016/j.spinee.2013.02.007]
- Hancock MJ, Maher CG, Latimer J, Spindler MF, McAuley JH, Laslett M, Bogduk N. Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *Eur Spine J* 2007; **16**: 1539-1550 [PMID: 17566796 DOI: 10.1007/s00586-007-0391-1]
- Alqarni AM, Schneiders AG, Cook CE, Hendrick PA. Clinical tests to diagnose lumbar spondylolysis and spondylolisthesis: A systematic review. *Phys Ther Sport* 2015; **16**: 268-275 [PMID: 25797410 DOI: 10.1016/j.ptsp.2014.12.005]
- Alqarni AM, Schneiders AG, Hendrick PA. Clinical tests to diagnose lumbar segmental instability: a systematic review. *J Orthop Sports Phys Ther* 2011; **41**: 130-140 [PMID: 21289452 DOI: 10.2519/jospt.2011.3457]
- May S, Littlewood C, Bishop A. Reliability of procedures used in the physical examination of non-specific low back pain: a systematic review. *Aust J Physiother* 2006; **52**: 91-102 [PMID: 16764546 DOI: 10.1016/S0004-9514(06)70044-7]
- Rebain R, Baxter GD, McDonough S. A systematic review of the passive straight leg raising test as a diagnostic aid for low back pain (1989 to 2000). *Spine (Phila Pa 1976)* 2002; **27**: E388-E395 [PMID: 12221373 DOI: 10.1097/01.BRS.0000025514.33588.65]
- Carlsson H, Rasmussen-Barr E. Clinical screening tests for assessing movement control in non-specific low-back pain. A systematic review of intra- and inter-observer reliability studies. *Man Ther* 2013; **18**: 103-110 [PMID: 23018080 DOI: 10.1016/j.math.2012.08.004]
- Cook C, Hegedus E. Diagnostic utility of clinical tests for spinal dysfunction. *Man Ther* 2011; **16**: 21-25 [PMID: 20685150 DOI: 10.1016/j.math.2010.07.004]
- Machado LA, Kamper SJ, Herbert RD, Maher CG, McAuley JH. Analgesic effects of treatments for non-specific low back pain: a meta-analysis of placebo-controlled randomized trials. *Rheumatology (Oxford)* 2009; **48**: 520-527 [PMID: 19109315 DOI: 10.1093/rheumatology/ken470]
- van Middelkoop M, Rubinstein SM, Kuijpers T, Verhagen AP, Ostelo R, Koes BW, van Tulder MW. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J* 2011; **20**: 19-39 [PMID: 20640863 DOI: 10.1007/s00586-010-1518-3]
- Rubinstein SM, van Middelkoop M, Kuijpers T, Ostelo R,

- Verhagen AP, de Boer MR, Koes BW, van Tulder MW. A systematic review on the effectiveness of complementary and alternative medicine for chronic non-specific low-back pain. *Eur Spine J* 2010; **19**: 1213-1228 [PMID: 20229280 DOI: 10.1007/s00586-010-1356-3]
- 27 **Kuijpers T**, van Middelkoop M, Rubinstein SM, Ostelo R, Verhagen A, Koes BW, van Tulder MW. A systematic review on the effectiveness of pharmacological interventions for chronic non-specific low-back pain. *Eur Spine J* 2011; **20**: 40-50 [PMID: 20680369 DOI: 10.1007/s00586-010-1541-4]
- 28 **Foster NE**. Barriers and progress in the treatment of low back pain. *BMC Med* 2011; **9**: 108 [PMID: 21943396 DOI: 10.1186/1741-7015-9-108]
- 29 **Foster NE**, Hill JC, O'Sullivan P, Hancock M. Stratified models of care. *Best Pract Res Clin Rheumatol* 2013; **27**: 649-661 [PMID: 24315146 DOI: 10.1016/j.berh.2013.10.005]
- 30 **Haskins R**, Osmotherly PG, Rivett DA. Diagnostic clinical prediction rules for specific subtypes of low back pain: a systematic review. *J Orthop Sports Phys Ther* 2015; **45**: 61-76, A1-A4 [PMID: 25573009 DOI: 10.2519/jospt.2015.5723]
- 31 **Haskins R**, Osmotherly PG, Rivett DA. Validation and impact analysis of prognostic clinical prediction rules for low back pain is needed: a systematic review. *J Clin Epidemiol* 2015; **68**: 821-832 [PMID: 25804336 DOI: 10.1016/j.jclinepi.2015.02.003]
- 32 **Fersum KV**, Dankaerts W, O'Sullivan PB, Maes J, Skouen JS, Bjordal JM, Kvåle A. Integration of subclassification strategies in randomised controlled clinical trials evaluating manual therapy treatment and exercise therapy for non-specific chronic low back pain: a systematic review. *Br J Sports Med* 2010; **44**: 1054-1062 [PMID: 19996331 DOI: 10.1136/bjism.2009.063289]
- 33 **Vibe Fersum K**, O'Sullivan P, Skouen JS, Smith A, Kvåle A. Efficacy of classification-based cognitive functional therapy in patients with non-specific chronic low back pain: a randomized controlled trial. *Eur J Pain* 2013; **17**: 916-928 [PMID: 23208945 DOI: 10.1002/j.1532-2149.2012.00252.x]
- 34 **Fairbank J**, Gwilym SE, France JC, Daffner SD, Dettori J, Hermesmeyer J, Andersson G. The role of classification of chronic low back pain. *Spine (Phila Pa 1976)* 2011; **36**: S19-S42 [PMID: 21952188 DOI: 10.1097/BRS.0b013e31822ef72c]
- 35 **Möller H**, Hedlund R. Surgery versus conservative management in adult isthmic spondylolisthesis--a prospective randomized study: part 1. *Spine (Phila Pa 1976)* 2000; **25**: 1711-1715 [PMID: 10870148]
- 36 **Jacobs WC**, Rubinstein SM, Koes B, van Tulder MW, Peul WC. Evidence for surgery in degenerative lumbar spine disorders. *Best Pract Res Clin Rheumatol* 2013; **27**: 673-684 [PMID: 24315148 DOI: 10.1016/j.berh.2013.09.009]
- 37 **Ammendolia C**, Stuber KJ, Rok E, Rampersaud R, Kennedy CA, Pennick V, Steenstra IA, de Bruin LK, Furlan AD. Nonoperative treatment for lumbar spinal stenosis with neurogenic claudication. *Cochrane Database Syst Rev* 2013; **8**: CD010712 [PMID: 23996271 DOI: 10.1002/14651858.CD010712]
- 38 **Saltychev M**, Eskola M, Laimi K. Lumbar fusion compared with conservative treatment in patients with chronic low back pain: a meta-analysis. *Int J Rehabil Res* 2014; **37**: 2-8 [PMID: 23820296 DOI: 10.1097/MRR.0b013e328363ba4b]
- 39 **Oosterhuis T**, Costa LO, Maher CG, de Vet HC, van Tulder MW, Ostelo RW. Rehabilitation after lumbar disc surgery. *Cochrane Database Syst Rev* 2014; **3**: CD003007 [PMID: 24627325 DOI: 10.1002/14651858.CD003007.pub3]
- 40 **Ozkara GO**, Ozgen M, Ozkara E, Armagan O, Arslantas A, Atasoy MA. Effectiveness of physical therapy and rehabilitation programs starting immediately after lumbar disc surgery. *Turk Neurosurg* 2015; **25**: 372-379 [PMID: 26037176 DOI: 10.5137/1019-5149.JTN.8440-13.0]
- 41 **Louw A**, Diener I, Landers MR, Puentedura EJ. Preoperative pain neuroscience education for lumbar radiculopathy: a multicenter randomized controlled trial with 1-year follow-up. *Spine (Phila Pa 1976)* 2014; **39**: 1449-1457 [PMID: 24875964 DOI: 10.1097/BRS.0000000000000444]
- 42 **McGregor AH**, Probyn K, Cro S, Doré CJ, Burton AK, Balagué F, Pincus T, Fairbank J. Rehabilitation following surgery for lumbar spinal stenosis. *Cochrane Database Syst Rev* 2013; **12**: CD009644 [PMID: 24323844 DOI: 10.1002/14651858.CD009644.pub2]
- 43 **Abbott AD**, Tyni-Lenné R, Hedlund R. Early rehabilitation targeting cognition, behavior, and motor function after lumbar fusion: a randomized controlled trial. *Spine (Phila Pa 1976)* 2010; **35**: 848-857 [PMID: 20354468 DOI: 10.1097/BRS.0b013e3181d1049f]
- 44 **Christensen FB**, Laurberg I, Bünger CE. Importance of the back-café concept to rehabilitation after lumbar spinal fusion: a randomized clinical study with a 2-year follow-up. *Spine (Phila Pa 1976)* 2003; **28**: 2561-2569 [PMID: 14652472]
- 45 **Monticone M**, Ferrante S, Teli M, Rocca B, Foti C, Lovi A, Brayda Bruno M. Management of catastrophising and kinesiophobia improves rehabilitation after fusion for lumbar spondylolisthesis and stenosis. A randomised controlled trial. *Eur Spine J* 2014; **23**: 87-95 [PMID: 23836299 DOI: 10.1007/s00586-013-2889-z]
- 46 **Nielsen PR**, Jørgensen LD, Dahl B, Pedersen T, Tønnesen H. Prehabilitation and early rehabilitation after spinal surgery: randomized clinical trial. *Clin Rehabil* 2010; **24**: 137-148 [PMID: 20103575 DOI: 10.1177/0269215509347432]
- 47 **Canbulat N**, Sasani M, Ataker Y, Oktenoglu T, Berker N, Ercelen O, Cerezci O, Ozer AF, Berker E. A rehabilitation protocol for patients with lumbar degenerative disk disease treated with lumbar total disk replacement. *Arch Phys Med Rehabil* 2011; **92**: 670-676 [PMID: 21367399 DOI: 10.1016/j.apmr.2010.10.037]
- 48 **Green A**, Gilbert P, Scott-Young M, Abbott A. Physiotherapeutic Rehabilitation Following Lumbar Total Disc Replacement: A Retrospective Study. *Physiother Res Int* 2015; Epub ahead of print [PMID: 25892105 DOI: 10.1002/pri.1630]

P- Reviewer: Tangtrakulwanich B, Yao DF

S- Editor: Ji FF L- Editor: A E- Editor: Li D



New regulations for medical devices: Rationale, advances and impact on research and patient care

Gerold Labek, Harald Schöffl, Christian Ioan Stoica

Gerold Labek, Department of Orthopaedic Surgery, Medical University of Innsbruck, 6020 Innsbruck, Austria

Harald Schöffl, Department for Trauma Surgery, General Hospital Linz, 4020 Linz, Austria

Christian Ioan Stoica, Clinica Fiosor de Foc, 060274 Bucharest, Romania

Author contributions: Labek G drafted, finalised and submitted the manuscript, carried out the literature review, contributed to the perspective of elective orthopaedic surgery, know-how from international register collaboration and as expert to regulators' working groups; Schöffl H provided content related to trauma surgery and implants and provided a critical review of the draft and final article; Stoica CI contributed through his experience as the Head of the Romanian Arthroplasty Register to the perspective from a national level and conducted a critical review of the draft and final article.

Conflict-of-interest statement: The authors have no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Gerold Labek, MD, Department of Orthopaedic Surgery, Medical University of Innsbruck, Innrain 52, 6020 Innsbruck, Austria. gerold.labek@i-med.ac.at
 Telephone: +43-512-50481600
 Fax: +43-512-50422701

Received: May 25, 2015

Peer-review started: May 27, 2015

First decision: June 26, 2015

Revised: December 7, 2015

Accepted: December 18, 2015

Article in press: December 21, 2015

Published online: March 18, 2016

Abstract

A series of events relating to inferior medical devices has brought about changes in the legal requirements regarding quality control on the part of regulators. Apart from clinical studies, register and routine data will play an essential role in this context. To ensure adequate use of these data, adapted methodologies are required as register data in fact represent a new scientific entity. For the interpretation of register and routine data several limitations of published data should be taken into account. In many cases essential parameters of study cohorts - such as age, comorbidities, the patients' risk profiles or the hospital profile - are not presented. Required data and evaluation procedures differ significantly, for example, between hip and spine implants. A "one fits for all" methodology is quite unlikely to exist and vigorous efforts will be required to develop suitable standards in the next future. The new legislation will affect all high-risk products, besides joint implants also contact lenses, cardiac pacemakers or stents, for example, the new regulations can markedly enhance product quality monitoring. Register data and clinical studies should not be considered as competitors, they complement each other when used responsibly. In the future follow-up studies should increasingly focus on specific questions, while global follow-up investigations regarding product complication rates and surgical methods will increasingly be covered by registers.

Key words: Arthroplasty; Outcome; Research; Medical device; Regulation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: In the next few years new worldwide regulations as well as the availability of register data will

lead to a shift in scientific focuses. The interpretation of register and routine data will be associated with new methodological challenges. Monocenter follow-up studies will become less attractive. Publications based on large data sets from registers will continue to gain influence and cover general issues; clinical studies should focus on specific questions.

Labek G, Schöffl H, Stoica CI. New regulations for medical devices: Rationale, advances and impact on research and patient care. *World J Orthop* 2016; 7(3): 162-166 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/162.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.162>

INTRODUCTION

Arthroplasty is one of the most successful interventions in terms of gain in quality of life^[1]. Nevertheless we must acknowledge the fact that about one in ten patients have to undergo revision surgery in the course of their life^[2]. Increasing age and the patients' growing confidence in the success of the operation are leading to rising numbers of cases. Moreover, patients are treated at an ever younger age, and even older patients increase their physical activity - and thus the strain on the implant. As a consequence, a marked future rise in revision surgeries has to be expected^[3].

Incidents with inferior products occurred at regular intervals in the past, with a significant number of patients harmed and great cost incurred by the healthcare system due to the necessity of revision surgeries. ASRTM and other metal-on-metal large diameter head implants, 3MTM hip system or cemented titanium stems are only a few examples^[4,5]. These problems are by no means restricted to joint implants only, but affect all groups of high-risk products, such as osteosynthesis devices, breast implants, contact lenses or cardiology products^[6-9]. It should therefore not come as a surprise that regulatory bodies like Food and Drug Administration or European Union Commission have taken initiatives to improve the situation as a whole, provide a higher level of safety to patients and physicians, and apart from personal suffering also reduce expenses in healthcare.

The experience of the past few years has shown that technical assessment, as well as the standard practice to evaluate outcome quality and potential risks of medical devices by means of sample-based clinical studies are insufficient^[10-12]. This is mainly due to some basic-medical device-specific-conditions, as well as to general structural weaknesses in the scientific system and the current evaluation procedures.

Limitations of the present system

Any of the current procedures is based on a standardized rating system for clinical evidence and studies with prospective randomized controlled Trials (RCT) considered as best study design. These standards pri-

marily take account of the circumstances that apply to pharmaceuticals. White tablets in anonymous boxes can easily be used in controlled and randomized circumstances; biological half-life allows a good estimate of the period of examination during which side effects have to be expected; persons collecting data can easily be blinded.

When it comes to implanted medical devices, this scheme reaches its limits. It is difficult to randomize surgical procedures, in many cases impossible due to ethical reasons. Placebo groups are unethical in general. Blinding of the physician who makes the decision and is responsible for documenting the study endpoint is hardly possible. For the standard endpoint Revision Rate this would, for instance, mean that the surgeon who decides on revision surgery and performs the intervention would neither be granted access to patient records nor to X-rays.

These limitations might be one reason for the low numbers of RCT's in orthopaedics. Since it is virtually impossible to estimate the time at which a complication occurs, the times for follow-up examinations and the duration of the study can hardly be determined prospectively. For example, if the lifespan of the battery of a pacemaker is three years, the problem would not be realized in a one-year study; at 5 years follow-up two years would have passed until measures can be taken - with patients being treated with a suboptimal product in the meantime. The logical approach of regular concomitant check-ups carries the risk of bias due to a break of the blinding and impact on the assessment of findings by discussing the evaluations performed; the methodological benefits of prospective study design would seriously be put into question.

Regardless of these limitations a systematic analysis of published results in regular clinical studies as compared to register data has revealed profound structural weaknesses in the current science system. About half of the implants examined in this worldwide meta-analysis of clinical studies showed statistically significant deviations of over 300% (as a measure of relevance in which deviations might also be explained by other factors, such as patient selection or the surgeon's expertise) compared with national register data as a measure for average patient care. Especially studies from the United States, as well as studies authored by implant developers were conspicuously often affected by implausibly good results. Marked differences were also found as to what was published in journals, for example, that on average 55% of cases published in orthopedic United States journals stem from implant developers, compared to only 7.5% in European journals^[13]. We must therefore accept that the present standards in scientific activities are susceptible to stakeholder influence, with a substantial impact on the opinion of orthopedic literature.

In principle the current standard of assessment gives very limited consideration to clinical studies. The primary objective of this assessment scheme is to restrict methodological shortcomings of sample-based studies. However, the concept neither gives full consideration

to the complete registration of all cases, as is largely achieved in good registers, nor does it allow for the specific requirements outlined above. Thus, a prospective randomized study of 50 patients would have to be classified as superior to a register evaluation of 50000 cases. Owing to the high standard in patient care, the endpoints of orthopedic studies, such as revision rate, are relatively rare. L.I. Havelin, one of the major co-founders of the Norwegian Arthroplasty Register, proved in his PhD thesis that in a conventional follow-up study nearly 15000 cases would be needed to determine a difference of 1 percentage point in the complication rate after 10 years. The relatively big effect of 2 percentage points would still require about 3000 patients. Therefore, the vast majority of published studies have to be considered as statistically underpowered, even if they are impeccable from a methodological point of view. In the 2010 comparative analysis of published clinical studies worldwide and the restricted number of high-quality national registers 80% of all cases available came from registers, only 20% from clinical studies^[13]. Now, five years later, the ratio has shifted to 90:10 percent. Considering that the National Joint Registry of England, Wales and Northern Ireland records more than 200000 cases per year, it is reasonable to assume that this data source will become increasingly important in the future.

Advances in future regulations and new challenges

In addition to a comprehensive presentation of all outcome quality data available, future legislation will also require a performance estimate within the scope of average patient care. This is supposed to address the problems associated with the fact that clinical studies are often conducted in centers of excellence, which are not representative for average use.

Improved monitoring shall include the product's entire lifetime, which can de facto only be covered by registers. Indicators for measuring embrace the whole treatment chain. Revision rate, the most important indicator for arthroplasty, in addition to product quality for example also includes the surgeon's quality, the patient's risk profile or general conditions of a healthcare system. Attribution of inferior outcome to a causer will be an essential factor as it defines at which stakeholder improvement measures can be launched. It is expected that this point will be an issue of controversial debate, particularly since responsibilities will be shared in many cases and serious legal and financial consequences may be involved. In the necessary decision-making process previous experience from register practice so far will be only of limited use. In past years and decades the interpretation of scientific data was largely a preserve of physicians. The data were published at congresses or in journal articles; that way critical debate was initiated within the expert audience, and physicians as the main decision-makers were expected to draw the consequences. Under these circumstances it makes sense to take action as early as a relevant problem is suspected. Regulators, authorities

or manufacturers, however, are bound to make clear and unambiguous decisions, such as recalling a product from the market - or not. This requires a higher level of reliability with regard to conclusions than is necessary for the discussion among experts. To ensure that the future procedures can actually meet the objectives of safety improvement, a number of issues have to be dealt with.

Issues to be addressed

Registers in principle are a new scientific entity which imposes special requirements on data collection and evaluation. One could compare the published annual reports, in some cases also journal publications, to clinical studies without "Materials and Methods". The patient cohorts included often are not or only insufficiently described, which may also be explained by the fact that the evaluations are chiefly addressed to physicians and other stakeholders of the respective country - who are usually familiar with the local circumstances. As the results are primarily intended for implementation in this particular area, the circumstances represent a constant and are therefore less important than for those readers who would like to apply the findings to other countries.

Even within the European Union the results of interventions show relevant differences in the population. Life expectancy, for instance, is about 10 years lower in some countries, such as Romania, than it is in Central European countries, or compared to Australia, for example, since the "positive outcome" of arthroplasty interventions effectively is the patient's death for another reason without the implant being revised, this is more probable for a 70-year-old Romanian than for a German, British or Australian of the same age. Therefore, registered differences in revision rate cannot be automatically interpreted as differences in the quality of treatment. The definition of relevant parameters for the final outcome and a structured description of the respective dataset would be useful to enable the reader to check whether the conclusions of a foreign register can be transferred to his or her own conditions.

Furthermore, the effects of the individual parameters should be quantified, which would be possible by comparative analyses of existing register datasets. The ultimate aim should be the standardization of data collection and evaluation procedures, at least when data from different registers are aggregated.

This can only be realized through international, if possible world-wide cooperation of registers, regulators, as well as the other stakeholders involved. Moreover, it would make sense to include the users of the data such as physicians and - beyond the narrow circle of register experts - product manufacturers or patients' mandatories. Open, transparent and democratic processes are of vital importance to ensure that the solutions to be elaborated receive social acceptance. As the results will have great influence on far-reaching decisions in patient care, careful and critical evaluation practice is a necessity. Risk adjustment regarding individual

factors and confounders is essential in the analysis of aggregated international data.

When going through foreign register data one should critically examine whether the results and conclusions could be affected by confounders and whether the basic data are representative for one's own area.

Future legislation is supposed to apply to all high-risk products. However, the pathologies, circumstances and aims these will be used for will vary greatly. Apart from joint implants, the range of products concerned also includes all permanently implanted orthopaedic devices, contact lenses, pacemakers, artificial cardiac valves or stents.

This inhomogeneity certainly has an impact on the evaluation and interpretation of the data, as well as on the conclusions drawn. Arthroplasty has acquired a leading position with regard to registers, not least because of favourable circumstances. The demand that no revision surgery should be required in the course of a patient's life after arthroplasty implantation is the basis for quality measurement. Any serious problem of or around the implant usually leads to revision surgery - which by definition is the "undesirable side effect" of the intervention. The procedure is performed in a hospital; comprehensive documentation is available for evaluations. Similar circumstances are true for a whole series of other medical devices, such as contact lenses, breast implants or pacemakers, but not for all. For a number of products, such as cardiac stents, mortality is the primary endpoint - and death may, but does not have to be associated with the use of a certain product. The removal of osteosynthesis devices or extension of a spinal fusion is not necessarily an undesired consequence of a primary intervention of insufficient quality. In the case of some products, for example, in shoulder and ankle arthroplasty, there are numerous patients who, in spite of unsatisfactory outcome, do not receive revision surgery. Thus, the endpoint of revision rate is meaningful only to a limited extent. In the future it will therefore be necessary to develop optimal solutions for every situation, "one fits for all" will hardly work.

Effects on patient care and science

The possibilities offered by the growing penetration of information technology in our working environment IT will lead to a rapid increase in routine data available. These provide a much better reflection of the reality of patient care than many clinical studies ever could since they are based on clearly defined patients and carried out by experienced surgeons under the favorable circumstances of centers of excellence. However, as medicine is anything but standardized - and presumably can hardly be standardized owing to the variability of patients and medical care - the transferability of results remains a relevant problem inherent to the system. Big data will become increasingly important in all our efforts to improve the quality of our services. Just like

in other areas of electronic data growing quantity does not automatically mean better quality. However, if dealt with and used critically, they open up new possibilities. In the process, certain study designs may become less important, such as simple follow-up studies with minor cohorts of a few hundred patients. The knowledge gained will hardly be able to compare favorably with register data and the usually considerably larger numbers of cases. Register evaluations, on the other hand, can only convey a relatively rough outline; the examination of detailed questions or treatment options will remain a domain of clinical studies. The cooperation of these two scientific tools can create added value, for example, when register data are used to adjust control groups more precisely. As many conventional follow-up studies are at present conducted for the purpose of the post-marketing clinical follow-up of products, it is likely that it will be less economic for implant manufacturers in the future to keep supporting this tool with the resources currently available. It is to be anticipated that budgets will be reallocated to registers on the one hand and clearly focussed clinical studies on the other hand in order to meet the requirements on the part of authorities and regulators. Most likely this will affect the way of implant development and acquisition of clinical evidence. Registries open opportunities for improvement by continuous feedback and outcome monitoring for manufacturers and implant designers. To assess detailed issues experimental, biomechanical and clinical studies will be essential, in premarket test phases as well as innovation circles.

CONCLUSION

Amended legislation in the quality assurance and monitoring of medical devices will allow for a marked improvement in patient safety and the quality of medical care. However, a number of methodological fundamentals for scientific assessment are still to be elaborated. While routine and register data are an increasingly important source of information, they will by no means supersede clinical studies but rather complement them. The time frames of scientific studies in orthopedics are often long; one should consider to make the necessary adjustments to the future situation now.

REFERENCES

- 1 **Learmonth ID**, Young C, Rorabeck C. The operation of the century: total hip replacement. *Lancet* 2007; **370**: 1508-1519 [PMID: 17964352 DOI: 10.1016/S0140-6736(07)60457-7]
- 2 **Labek G**, Thaler M, Janda W, Agreiter M, Stöckl B. Revision rates after total joint replacement: cumulative results from worldwide joint register datasets. *J Bone Joint Surg Br* 2011; **93**: 293-297 [PMID: 21357948 DOI: 10.1302/0301-620X.93B3.25467]
- 3 **Kurtz SM**, Ong KL, Schmier J, Mowat F, Saleh K, Dybvik E, Kärrholm J, Garellick G, Havelin LI, Furnes O, Malchau H, Lau E. Future clinical and economic impact of revision total hip and knee arthroplasty. *J Bone Joint Surg Am* 2007; **89** Suppl 3: 144-151 [PMID: 17908880 DOI: 10.2106/JBJS.G.00587]
- 4 **Furnes O**, Paxton E, Cafri G, Graves S, Bordini B, Comfort T,

- Rivas MC, Banerjee S, Sedrakyan A. Distributed analysis of hip implants using six national and regional registries: comparing metal-on-metal with metal-on-highly cross-linked polyethylene bearings in cementless total hip arthroplasty in young patients. *J Bone Joint Surg Am* 2014; **96** Suppl 1: 25-33 [PMID: 25520416 DOI: 10.2106/JBJS.N.00459]
- 5 **Roy N**, Hossain S, Ayeko C, McGee HM, Elsworth CF, Jacobs LG. 3M Capital hip arthroplasty: 3-8-year follow-up of 208 primary hip replacements. *Acta Orthop Scand* 2002; **73**: 400-402 [PMID: 12358111 DOI: 10.1080/00016470216328]
- 6 **Food and Drug Administration**. MedWatch: The FDA Safety Information and Adverse Event Reporting Program. [updated 2014 Aug 15]. Available from: URL: <http://www.fda.gov/Safety/MedWatch/default.htm>
- 7 **Food and Drug Administration**. Safety of Specific Products. [updated 2015 Feb 11]. Available from: URL: <http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/>
- 8 **Therapeutic Goods Administration**. PIP breast implants - an updated Australian perspective. [updated 2012 Mar 13]. Available from: URL: <http://www.tga.gov.au/alert/pip-breast-implants-updated-australian-perspective>
- 9 **Medicines and Healthcare Products Regulatory Agency**. Alerts and recalls for drugs and medical devices. Available from: URL: <http://www.gov.uk/drug-device-alerts>
- 10 **Godlee F**. The trouble with medical devices. *BMJ* 2011; **342**: d3123 [DOI: 10.1136/bmj.d3123]
- 11 **Sedrakyan A**. Hip resurfacing: a complex challenge for device regulation. *Lancet* 2012; **380**: 1720-1722 [PMID: 23036898 DOI: 10.1016/S0140-6736(12)61270-7]
- 12 **Sedrakyan A**. Metal-on-metal failures-in science, regulation, and policy. *Lancet* 2012; **379**: 1174-1176 [PMID: 22417409 DOI: 10.1016/S0140-6736(12)60372-9]
- 13 **Abek G**. QoLA-Project final report. Available from: URL: <http://www.ear.efort.org/>

P- Reviewer: Cui QT, Fisher DA, Guerado E, Hasegawa M, Kodde IF
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D



Entrapment of middle cluneal nerves as an unknown cause of low back pain

Yoichi Aota

Yoichi Aota, Department of Spine and Spinal Cord Surgery, Yokohama Brain and Spine Center, Yokohama 235-0012, Kanagawa Prefecture, Japan

Author contributions: Aota Y conceived the issues which formed the content of the manuscript and wrote the manuscript.

Conflict-of-interest statement: The author has no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Yoichi Aota, MD, Department of Spine and Spinal Cord Surgery, Yokohama Brain and Spine Center, Takigashira 1-2-1, Isogo-ku, Yokohama 235-0012, Kanagawa Prefecture, Japan. yaota@yokohama-cu.ac.jp
Telephone: +81-45-7532500
Fax: +81-45-7532859

Received: September 6, 2015
Peer-review started: September 8, 2015
First decision: October 16, 2015
Revised: October 17, 2015
Accepted: December 18, 2015
Article in press: December 21, 2015
Published online: March 18, 2016

Abstract

Entrapment of middle cluneal nerves induces low back pain and leg symptoms. The middle cluneal nerves can become spontaneously entrapped where this nerve pass under the long posterior sacroiliac ligament. A case of severe low back pain, which was completely

treated by release of the middle cluneal nerve, was presented. Entrapment of middle cluneal nerves is possibly underdiagnosed cause of low-back and/or leg symptoms. Spinal surgeons should be aware of this clinical entity and avoid unnecessary spinal surgeries and sacroiliac fusion. This paper is to draw attention by pain clinicians in this unrecognized etiology.

Key words: Entrapment neuropathy; Superior cluneal nerve; Middle cluneal nerve; Sacroiliac joint; Low back pain; Neuropathic pain

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A case of severe low back pain, which was completely treated by release of the middle cluneal nerve, was presented. Clunealgia is underdiagnosed cause of low back pain and leg pain. The middle cluneal nerve may be entrapped where this nerve pass under or through the long posterior sacroiliac ligament.

Aota Y. Entrapment of middle cluneal nerves as an unknown cause of low back pain. *World J Orthop* 2016; 7(3): 167-170 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/167.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.167>

INTRODUCTION

Recently, clunealgia has become known as an underdiagnosed cause for chronic low back pain (LBP) or leg pain^[1-5]. Trescot^[2] stated that cluneal neuralgia is more commonly the result of an entrapped nerve rather than a nerve injury resulting from iliac crest bone harvest. Kuniya *et al*^[3] reported that patients with superior cluneal nerve (SCN) entrapment occurs where pierce fascial attachment at posterior iliac crest. SCN disorders comprised 12% of all patients presenting with a chief

complaint of LBP and/or leg symptoms in their clinic and approximately 50% of SCN disorder patients had leg pain and/or tingling.

The concept of a relationship between the cluneal nerve and LBP is not new. A relationship between the cluneal nerve and LBP was sporadically reported several decades ago^[6,7]. The first detailed description was made by Strong *et al*^[7] in 1957. Deafferentation of the SCN and/or middle cluneal nerve (MCN) was attempted in 30 patients because these nerves were considered to cause LBP with or without referred leg pain. Of 30 patients, five had referred pain in their leg in the S1 and/or S2 area and had deafferentation of the MCN with favorable outcomes.

Maigne *et al*^[8] and Lu *et al*^[4] performed cadaveric dissections to study anatomy of the SCN and concluded that the medial branch of the SCN consistently passed through an osteofibrous tunnel and might be spontaneously entrapped in the tunnel. Following these anatomical studies, several surgeons reported successful surgical outcomes of SCN release^[3,5,9]. However, surgical reports of release are limited to SCN entrapment. Until now, MCN entrapment has not yet been reported in English literature. This paper is to firstly present a case of MCN entrapment and to draw attention by pain clinicians in MCN entrapment.

CASE REPORT

In April 2013, a 48-year-old woman presented complaining of LBP and buttock pain radiating to both legs that had gradually developed over 10 years. L4-5 discectomy performed at another hospital two years before resulted in no improvement. The pain was continuous and severe even with long-term daily use of tramadol 225 mg/acetaminophen 1950 mg, pregabalin 50 mg and loxoprofen sodium 180 mg. The visual analog scale (VAS) score was 67 mm and the Roland-Morris Disability Questionnaire (RDQ) score was 18. A neurologic examination revealed no sensory or motor disturbance in her legs. Lumbar motion was greatly limited in all directions because of pain (Appendix, video 1). The finger floor distance in flexion was 50 cm. Palpation of the superior SCN tender point, located 7 cm laterally to the midline on the bilateral iliac crest^[7], replicated the postero-lateral aspect of calf pain. She also had significant tender points approximately 1.5 cm caudal to the palpable margin of the bilateral posterior superior iliac spine, by the lateral sides of the long posterior sacroiliac ligament (LPSL). These loci were along the running course of the MCN as described in an anatomical report by Tubbs *et al*^[10]. Palpation of MCN tender points provoked mid-posterior thigh pain. Repetitive infiltration of a local anesthetic, Lidocaine, into each tender point consistently resulted in clear improvement of symptoms for three hours.

The patient was informed that release was previously performed exclusively for SCN entrapment and had never been applied for MCN entrapment. She gave their

informed consent to undergo surgical decompression. In May 2013, microscopic SCN and MCN releases were attempted. Surgeries were approved by the Institutional Ethics Committee of our institution. Surgery was performed bilaterally under general anesthesia with the patient in the prone position. An oblique 10 cm skin incision was made over the iliac crests. Being careful not to injure nerve branches passing through subcutaneous tissues, the superficial layer of the thoracolumbar fascia was opened. Two branches of the SCN were identified within 5 cm above the iliac crest and were seen to emerge from the lateral margin of the deep layer of the thoracolumbar fascia. These SCN branches were traced in a caudal direction until they passed over the iliac crest. In agreement with a recent anatomical study, the two medial branches of the SCN where they pierce the thoracolumbar fascia over the iliac crest were found to be entrapped in adhesions. A thin branch of the MCN perforating the thoracolumbar fascia was identified just medial to the posterior superior iliac spines. Although obvious entrapment was not observed, the perforating orifices were opened.

Within one week following surgery, the patient reported that her pain had completely disappeared around the upper iliac crests, but remained around the LPSL on both sides. Palpation on the LPSL consistently induced LBP and leg tingling radiating from the buttocks to the calves on both sides. Injections around the LPSL were repeated every month. Each time, the patient reported reappearance of leg tingling during the block procedure and, soon after, complete improvement in LBP and leg tingling that continued for three days. Consequently, blocks were repeated six times over six months without substantial permanent change in LBP. The VAS score was 50 mm at six months after surgery. Near-full range of flexion was obtained with no pain reappearance, but lumbar extension was still severely limited.

In an attempt to eliminate remaining pain, in December 2013, revision surgery was done. Previous operative incisions were reopened. After gluteal muscle splitting approach, the bilateral MCNs were explored where the nerves penetrate the LPSL (Figure 1). Proximally, the nerves possibly arose from the S2 foramen. The MCNs were decompressed by excising the LPSL where the nerve penetrates the ligament. After revision, pain dramatically improved, precluding need for any medication. The patient had no limitation in lumbar motion. The VAS score at eight months after revision was 0 mm and the RDQ score was 1.

DISCUSSION

The MCN is composed of sensory branches of the dorsal rami of S1 to S3 foramina and travels below the PSIS in an approximately horizontal course to supply the skin overlying the posteromedial area of the buttock^[10-12]. The evidence that predominantly the S1 and S2 lateral branches may explain why MCN disorder could cause leg symptoms in posterior thigh to calf.

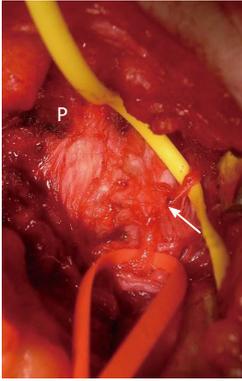


Figure 1 Photo taken during the surgical release of a left-side middle cluneal nerve. Medially to the posterior superior iliac crest (P), the MCN is identified passing under the superficial layer of the long posterior sacroiliac ligament. The nerve is seen to be entrapped under the deeper layer of the long posterior sacroiliac ligament where it penetrates the ligament (arrow). The yellow and red tapes have been used to lift the proximal and distal portions of MCN branch, respectively. MCN: Middle cluneal nerve.

Tubbs *et al*^[10] studied anatomy running course of MCN and concluded that the MCN would be less likely to become entrapped because MCN travels superficial to the LPSL. On the other hand, anatomical studies by Horwitz^[13], Grob *et al*^[12], and McGrath *et al*^[14] showed that the primary and secondary loops of the posterior sacral nerve plexus passed through or underneath the LPSL. They suggested entrapment of the penetrating nerves within or under the ligament is a potential cause for LBP and peripartum pelvic pain.

A diagnosis of SCN/MCN entrapment was made by palpation of the iliac crest or LPSL resulting in marked tenderness and provocation of symptoms, and by pain relief after local anesthetic injection. The SCN tender point was on the posterior iliac crest approximately 70 mm from the midline and 45 mm from the PSIS^[3]. The MCN tender point was on the LPSL within 40 mm caudal to the PSIS (Figure 2).

Pain due to MCN entrapment may be treated as sacroiliac joint pain. Although sacroiliac joint pain remains a controversial subject, it is thought to cause 15% to 30% of LBP and is often associated with buttock to lower extremity symptoms^[15]. There are no medical history or physical examination findings consistently capable of identifying sacroiliac joint pain^[16]. The physical examination tests, such as Patrick's test or Gaenslen's test, have weak predictive value^[15]. Radiological imaging contributes little to diagnosis^[15]. The current gold standard for the diagnosis is fluoroscopically guided sacroiliac joint blocks^[15]. Fortin *et al*^[17] analyzed contrast extravasation patterns during 76 sacroiliac joint arthrograms by using computerized tomography and found dorsal leakage around LPSL in 18 cases (24%) and dorsal leakage into the S1 foramen in 6 (8%) The LPSL is a significant posterior ligamentous structure, resisting shearing of the sacroiliac joint and is a potential pain generator^[14,18]. Murakami *et al*^[19] compared the effect of injections into the intraarticular space and periarticular region around

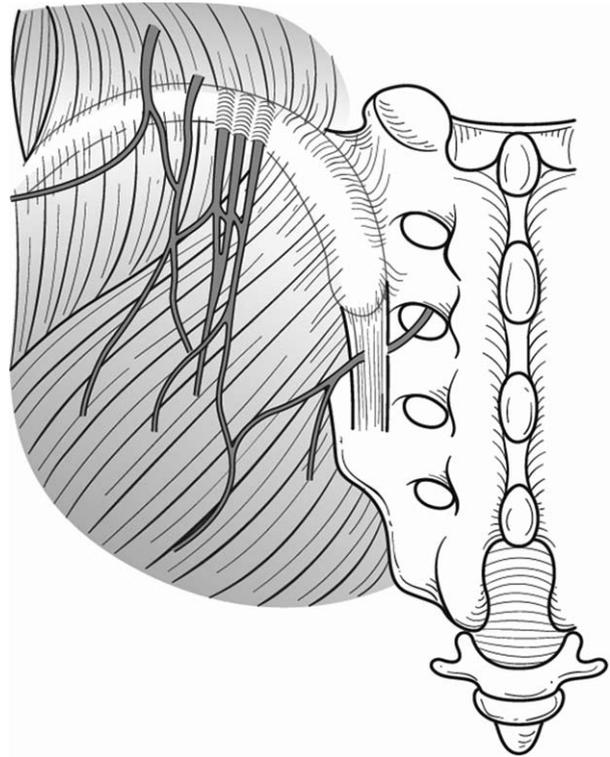


Figure 2 Schematic illustration of typical running courses and entrapment of superior and middle cluneal nerves. Multiple branches of the superior cluneal nerve may be entrapped where they pierce the thoracolumbar fascia over the iliac crest. Middle cluneal nerve may be entrapped where this nerve pass under or through the long posterior sacroiliac ligament.

the LPSL in patients with sacroiliac joint pain. The injection around the LPSL was effective in all 25 patients, whereas the intraarticular injection was effective in only nine out of 25 patients (36%). Furthermore, all 16 patients without pain relief after the intraarticular injection reported almost complete pain relief after injection around the LPSL. Fortin *et al*^[16] stated that sacroiliac joint patients could localize their pain with one finger and the area pointed to was immediately inferomedial to the posterior superior iliac spine within 1 cm. Murakami *et al*^[20] observed a positive effect with periarticular sacroiliac joint block in 18 patients out of 25 patients who indicated the main site of pain within 2 cm of the posterior superior iliac spine. These results suggest that sacroiliac joint pain can originate from the LPSL^[20].

LBP is one of the most common problems that most people suffer at some point in their life. There are many sources of LBP. In most LBP patients, the exact cause of LBP is not clear. Thus, one of the most difficult tasks with LBP is to identify the actual pain generator. Large epidemiological studies show that 20% to 37% of patients with back pain suffer from a neuropathic pain component^[21]. So far, neuropathic pain is considered to be caused by lesions of nociceptive sprouts within the degenerated disc, mechanical compression of the nerve root, or by action of inflammatory mediators originating from the degenerative disc^[22]. SCN/ MCN entrapment must not be forgotten as cause of neuropathic LBP.

CONCLUSION

MCN entrapment is underdiagnosed cause of low back pain and leg pain. For a structure to be considered as a potential source of pain, pain must be provoked by palpation or relieved by local anesthetic injection of the tender point around LPSL. Knowledge of this clinical entity would avoid unnecessary sacroiliac joint fusion and spinal surgeries.

REFERENCES

- 1 Akbas M, Yegin A, Karsli B. Superior cluneal nerve entrapment eight years after decubitus surgery. *Pain Pract* 2005; **5**: 364-366 [PMID: 17177772 DOI: 10.1111/j.1533-2500.2005.00040.x]
- 2 Trescot AM. Cryoanalgesia in interventional pain management. *Pain Physician* 2003; **6**: 345-360 [PMID: 16880882]
- 3 Kuniya H, Aota Y, Kawai T, Kaneko K, Konno T, Saito T. Prospective study of superior cluneal nerve disorder as a potential cause of low back pain and leg symptoms. *J Orthop Surg Res* 2014; **9**: 139 [PMID: 25551470 DOI: 10.1186/s13018-014-0139-7]
- 4 Lu J, Ebraheim NA, Huntoon M, Heck BE, Yeasting RA. Anatomic considerations of superior cluneal nerve at posterior iliac crest region. *Clin Orthop Relat Res* 1998; (347): 224-228 [PMID: 9520894 DOI: 10.1097/00003086-199802000-00027]
- 5 Maigne JY, Doursounian L. Entrapment neuropathy of the medial superior cluneal nerve. Nineteen cases surgically treated, with a minimum of 2 years' follow-up. *Spine (Phila Pa 1976)* 1997; **22**: 1156-1159 [PMID: 9160476 DOI: 10.1097/00007632-199705150-00017]
- 6 Drury BJ. Clinical evaluation of damage to the superior cluneal nerves. *Am J Orthop Surg* 1968; **10**: 102-106 [PMID: 4297034]
- 7 Strong EK, Davila JC. The cluneal nerve syndrome; a distinct type of low back pain. *Ind Med Surg* 1957; **26**: 417-429 [PMID: 13462591]
- 8 Maigne JY, Maigne R. Trigger point of the posterior iliac crest: painful iliolumbar ligament insertion or cutaneous dorsal ramus pain? An anatomic study. *Arch Phys Med Rehabil* 1991; **72**: 734-737 [PMID: 1834038]
- 9 Morimoto D, Isu T, Kim K, Imai T, Yamazaki K, Matsumoto R, Isobe M. Surgical treatment of superior cluneal nerve entrapment neuropathy. *J Neurosurg Spine* 2013; **19**: 71-75 [PMID: 23621641 DOI: 10.3171/2013.3.SPINE12420]
- 10 Tubbs RS, Levin MR, Loukas M, Potts EA, Cohen-Gadol AA. Anatomy and landmarks for the superior and middle cluneal nerves: application to posterior iliac crest harvest and entrapment syndromes. *J Neurosurg Spine* 2010; **13**: 356-359 [PMID: 20809730 DOI: 10.3171/2010.3.SPINE09747]
- 11 Sittitavornwong S, Falconer DS, Shah R, Brown N, Tubbs RS. Anatomic considerations for posterior iliac crest bone procurement. *J Oral Maxillofac Surg* 2013; **71**: 1777-1788 [PMID: 23623198 DOI: 10.1016/j.joms.2013.03.008]
- 12 Grob KR, Neuhuber WL, Kissling RO. [Innervation of the sacroiliac joint of the human]. *Z Rheumatol* 1995; **54**: 117-122 [PMID: 7793158]
- 13 Horwitz TM. The anatomy of (a) the lumbosacral nerve plexus - its relation to variations of vertebral segmentation, and (b) the posterior sacral nerve plexus. *Anat Rec* 1939; **74**: 91-107 [DOI: 10.1002/ar.1090740110]
- 14 McGrath MC, Zhang M. Lateral branches of dorsal sacral nerve plexus and the long posterior sacroiliac ligament. *Surg Radiol Anat* 2005; **27**: 327-330 [PMID: 16237486 DOI: 10.1007/s00276-005-0331-x]
- 15 Vanelderen P, Szadek K, Cohen SP, De Witte J, Lataster A, Patijn J, Mekhail N, van Kleef M, Van Zundert J. 13. Sacroiliac joint pain. *Pain Pract* 2010; **10**: 470-478 [PMID: 20667026 DOI: 10.1111/j.1533-2500.2010.00394.x]
- 16 Fortin JD, Falco FJ. The Fortin finger test: an indicator of sacroiliac pain. *Am J Orthop (Belle Mead NJ)* 1997; **26**: 477-480 [PMID: 9247654]
- 17 Fortin JD, Washington WJ, Falco FJ. Three pathways between the sacroiliac joint and neural structures. *AJNR Am J Neuroradiol* 1999; **20**: 1429-1434 [PMID: 10512224]
- 18 Vleeming A, Pool-Goudzwaard AL, Hammudoghlu D, Stoeckart R, Snijders CJ, Mens JM. The function of the long dorsal sacroiliac ligament: its implication for understanding low back pain. *Spine (Phila Pa 1976)* 1996; **21**: 556-562 [PMID: 8852309 DOI: 10.1097/00007632-199603010-00005]
- 19 Murakami E, Tanaka Y, Aizawa T, Ishizuka M, Kokubun S. Effect of periarticular and intraarticular lidocaine injections for sacroiliac joint pain: prospective comparative study. *J Orthop Sci* 2007; **12**: 274-280 [PMID: 17530380 DOI: 10.1007/s00776-007-1126-1]
- 20 Murakami E, Aizawa T, Noguchi K, Kanno H, Okuno H, Uozumi H. Diagram specific to sacroiliac joint pain site indicated by one-finger test. *J Orthop Sci* 2008; **13**: 492-497 [PMID: 19089535 DOI: 10.1007/s00776-008-1280-0]
- 21 Freynhagen R, Baron R, Gockel U, Tölle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006; **22**: 1911-1920 [PMID: 17022849 DOI: 10.1185/030079906X132488]
- 22 Freynhagen R, Baron R. The evaluation of neuropathic components in low back pain. *Curr Pain Headache Rep* 2009; **13**: 185-190 [PMID: 19457278 DOI: 10.1007/s11916-009-0032-y]

P- Reviewer: Feher G, Peng BG S- Editor: Qiu S

L- Editor: A E- Editor: Li D



Major osteoporotic fragility fractures: Risk factor updates and societal impact

Paola Pisani, Maria Daniela Renna, Francesco Conversano, Ernesto Casciaro, Marco Di Paola, Eugenio Quarta, Maurizio Muratore, Sergio Casciaro

Paola Pisani, Maria Daniela Renna, Francesco Conversano, Ernesto Casciaro, Marco Di Paola, Sergio Casciaro, National Council of Research, Institute of Clinical Physiology, 73100 Lecce, Italy

Eugenio Quarta, Maurizio Muratore, O.U. of Rheumatology, "Galateo" Hospital, San Cesario di Lecce, ASL-LE, 73100 Lecce, Italy

Author contributions: All the authors were involved in designing the study and writing the manuscript.

Supported by FESR P.O. Apulia Region 2007-2013 - Action 1.2.4, No. 3Q5AX31.

Conflict-of-interest statement: No potential conflicts of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Sergio Casciaro, PhD, Eng, National Council of Research, Institute of Clinical Physiology, (CNR-IFC), c/o Campus Universitario Ecotekne, via per Monteroni, 73100 Lecce, Italy. sergio.casciaro@cnr.it
Telephone: +39-0832-422310
Fax: +39-0832-422341

Received: July 10, 2015

Peer-review started: July 24, 2015

First decision: September 22, 2015

Revised: November 14, 2015

Accepted: December 7, 2015

Article in press: December 8, 2015

Published online: March 18, 2016

Abstract

Osteoporosis is a silent disease without any evidence of disease until a fracture occurs. Approximately 200 million people in the world are affected by osteoporosis and 8.9 million fractures occur each year worldwide. Fractures of the hip are a major public health burden, by means of both social cost and health condition of the elderly because these fractures are one of the main causes of morbidity, impairment, decreased quality of life and mortality in women and men. The aim of this review is to analyze the most important factors related to the enormous impact of osteoporotic fractures on population. Among the most common risk factors, low body mass index; history of fragility fracture, environmental risk, early menopause, smoking, lack of vitamin D, endocrine disorders (for example insulin-dependent diabetes mellitus), use of glucocorticoids, excessive alcohol intake, immobility and others represented the main clinical risk factors associated with augmented risk of fragility fracture. The increasing trend of osteoporosis is accompanied by an underutilization of the available preventive strategies and only a small number of patients at high fracture risk are recognized and successively referred for therapy. This report provides analytic evidences to assess the best practices in osteoporosis management and indications for the adoption of a correct healthcare strategy to significantly reduce the osteoporosis burden. Early diagnosis is the key to reduce the impact of osteoporosis on healthcare system. In this context, attention must be focused on the identification of high fracture risk among osteoporotic patients. It is necessary to increase national awareness campaigns across countries in order to reduce the osteoporotic fractures incidence.

Key words: Fracture prevention; Fracture risk; Fragility fracture; Osteoporosis; Hip fracture

© The Author(s) 2016. Published by Baishideng Publishing

Group Inc. All rights reserved.

Core tip: The osteoporosis burden is growing and 9 million fractures occur each year worldwide. Unfortunately, because of the underutilization of available preventive strategies, only a minority of women and men at high fracture risk are identified and successively referred for treatment. The aim of this review is to analyze the most important factors related to the enormous impact of osteoporotic fractures on population. Because early diagnosis is the key to reduce the impact of osteoporosis on healthcare system, attention must be focused on the identification of high fracture risk among osteoporotic patients.

Pisani P, Renna MD, Conversano F, Casciaro E, Di Paola M, Quarta E, Muratore M, Casciaro S. Major osteoporotic fragility fractures: Risk factor updates and societal impact. *World J Orthop* 2016; 7(3): 171-181 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/171.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.171>

INTRODUCTION

Osteoporosis has been defined as a systemic disease which affects the skeleton and is characterized by low bone mass, deterioration of microarchitecture of bone tissue and bone fragility increase with consequent susceptibility to fracture^[1].

This bone pathology can be classified in primary or secondary forms. Primary osteoporosis is characterized by a progressive mineral bone lost as a function of people aging and it is influenced by changes of sex hormone. Instead, different pathologies as well as the use of specific medications, which affect skeletal health, can induce secondary osteoporosis. Primary form of osteoporosis comprises postmenopausal or senile disease (type I or type II respectively)^[2]. Type I osteoporosis takes place in a subgroup of postmenopausal women, usually aged from 50 to 65 years, due to estrogen deficiency and consequent trabecular bone resorption. In this set of women fracture pattern mainly involves the spine and wrist. There is no evidence that postmenopausal bone loss itself causes any symptoms, and therefore, progressive bone loss has been called "the silent epidemic" or "silent thief". The morbidity arises from the type of fracture sustained^[3]. In senile osteoporosis, there is a balanced loss of both cortical and cancellous portions of bone tissue. Fractures of the hip, proximal humerus, tibia, and pelvis represent characteristic fractures of type II osteoporosis^[4].

Although osteoporosis has long been considered a disease of women, an increase in age-related fractures has been observed also in men^[5]. Nowadays, the number of males with osteoporosis is unknown, probably because of the infrequency of screening and controversies in bone mineral density (BMD) testing standards in men.

Approximately the 50% of women and the 25% of men aged 50 and older will have an osteoporotic fracture in the lifetime^[6]. Although many national and international organizations indicate to realize osteoporosis screening and treatment for men in their clinical guidelines, male osteoporosis remains recurrently not diagnosed and not treated^[7,8].

The high socio-economic impact of osteoporosis is due to increased incidence of the disease, mortality and fracture-related costs. The occurrence of osteoporotic fractures is growing in several world areas as a consequence of the increased longevity of the population. Indeed, the number of hip fracture worldwide has reached 1.7 million by 1990^[9,10]. In 2050, hip fractures could exceed 21 million^[10,11]. In this context, attention must be focused on the identification of high fracture risk patients^[12]. There is, therefore, the strong need to assess the best preventive methods and therapeutic approaches to contrast fracture widening across populations. A large number of techniques can be used to assess the risk of fracture. In general, they fall into two major categories: Assessment of clinical risk factors (CRFs) and physical measurement of skeletal mass. Nowadays, the assessment of osteoporosis is based on bone density evaluation, and there are no satisfying clinical approaches, independent of BMD, for bone quality estimation^[3].

The aim of this review is to analyze the main factors causing the huge impact of osteoporosis on the population, and to stress the importance of risk factors recognition and early identification of fracture risk in order to discriminate frail patients from non-frail patients. Currently, only a small number of high fracture risk patients are recognized and successively referred for therapy. In this context, the present report provides analytic evidences to assess the best practices in osteoporosis management as well as the indications for the adoption of a correct healthcare approach to decrease the socio-economic burden of osteoporosis.

FRACTURE RISK ASSESSMENT

Assessment of CRFs

A list of risk factors has been determined (Table 1) both for women and men. In several instances, exist a clear relationship between these risk factors and low bone density or other causes of osteoporotic fractures.

In recent years, there have been a number of advances, principally in BMD measurement, osteoporosis diagnosis, fracture risk evaluation, the development of interventions that decrease risk of fractures and the creation of practice guidelines. Recently, a set of meta-analyses have been carried out to recognize CRFs to use in case finding strategies with or without the use of BMD. These are summarized below together with risk factors for falling because the majority of osteoporosis-related fractures derive from falls^[13].

An important risk factor for hip fracture is low body mass index (BMI). Thus, the risk is nearly two-fold

Table 1 Clinical risk factors associated with increased risk of fragility fracture

Risk factors associated with low BMD and fracture	Risk factors for falls
For woman as for men	
¹ Increased age	Age
¹ Low BMI	Environmental risk
¹ History of fragility fractures	Previous falls
¹ Previous fragility fractures	Dehydration
¹ Parental history of fragility fractures	Depression
Recent falls	Poor vision
¹ Premature menopause	Sarcopenia
¹ Untreated hypogonadism	Urgent urinary incontinence
Poor neuromuscular function	Malnutrition
¹ Prolonged immobilization and inactivity	Neurological risk factors
¹ Alcohol intake	
¹ Current smoking	
¹ Glucocorticoids treatment (≥ 5 mg prednisolone daily for 3 mo or more)	
¹ Type I diabetes (and other endocrine disorders)	
Vitamin D insufficiency	
¹ Rheumatoid arthritis (and other rheumatologic diseases)	
Aromatase inhibitor for breast cancer treatment	
Chemotherapy for breast cancer	
¹ Thyroid disorders	
Chronic obstructive pulmonary disease	
Anorexia nervosa (and other hypogonadal states)	
Depressed mood	
Tricyclic antidepressant use	
Stroke	
IBD and other gastrointestinal disorders	
Organ transplantation	
Hematologic disorders	
Neurological and musculoskeletal risks	

Adapted from Cosman *et al*^[13] with modification. ¹CRFs for fracture risk assessment from tool FRAX[®]. BMD: Bone mineral density; CRFs: Clinical risk factors; IBD: Inflammatory bowel diseases; BMI: Body mass index.

increased for individuals with a BMI of 25 kg/m² vs 20 kg/m²^[14-17]. Numerous studies show that a history of fragility fracture represent an important risk factor for further fracture independently of BMD^[1,18,19]. It was shown that the risk of fracture is around doubled in the presence of a prior fracture^[1,20].

Early menopause (before age 45 years), both natural and surgically induced, leads to an increased risk of mortality and fragility fractures^[21] because these women are exposed to a hypogonadal state for a longer time^[3].

Similarly, many abnormalities of menstrual function as well as late menarche and primary or secondary amenorrhea might also contribute to low BMD and therefore also increase the risk of osteoporosis^[3,22,23]. Hypogonadism also occurs in a small proportion of men and might lead to bone loss^[24] and fractures^[25]. Postmenopausal women are capable of producing adrenal steroids, of which androstenedione is converted to estrogens in adipose tissue. This might explain why thin women are at greater risk than their heavier counterparts, and possibly because smoking, which decreases appetite and body fat, is a risk factor^[3]. There might be, however, additional factors related to smoking, and there is some evidence that smoking might accelerate the peripheral metabolism of exogenously administered estrogen^[26]. Moreover, because female cigarette smokers are thinner than non-smokers, they have an earlier natural menopause^[3].

On one hand crucial role for estrogen in bone loss is indicated by the increasing resorption of bone at menopause^[5,27,28]; on the other hand, in men, although total serum testosterone and estrogen levels not vary with increasing age, the bioavailability fractions decrease progressively to 30%-50% of the young adults average after 80 years of age^[5,29].

Lack of vitamin D is another risk factor. It is well known that vitamin D, calcium and protein insufficiency is highly frequent in the elderly. Vitamin D deficiency in adults can aggravate osteopenia and osteoporosis, and causes osteomalacia and muscle weakness, increasing the risk of fracture. Vitamin D can be obtained from diet or exposure to sunlight. Solar ultraviolet B radiation (wavelength, 290-315 nm) can convert 7-dehydrocholesterol to previtamin D3 and consequently to vitamin D3 by penetrating the skin. Vitamin D deficiency and bone fragility are also common in some countries such as Iran, where conservative cultural codes encourage body coverage and so limit sun exposure^[30].

In addition to vitamin D insufficiency, hyperthyroidism and secondary hyperparathyroidism also take part in particular to age-related cortical bone loss in the elderly^[31]. Other probable pathogenetic aspects comprise reduced serum levels of insulin-like growth factors^[32]. Age-related bone loss and reduced bone strength (due to the imbalance between the activities of osteoblasts and

the osteoclasts) are believed to start in both men and women from the beginning of the 5th decade until the end of life^[33]. It is also possible that some early factors (*i.e.*, perinatal nutrition) have affected the successive late-life risk of fractures in adults^[8,34,35].

Bone loss is due to many disorders, such as insulin-dependent diabetes mellitus and Cushing's disease. Myelomatosis might be present with osteoporotic crush. Rarer causes of osteoporosis include osteogenesis imperfecta, malabsorption, chronic renal failure and some drugs. However, all these disorders are comparatively rare and have relatively little impact upon any general screening strategy^[3].

Other secondary causes of osteoporosis are linked with an increase in fracture risk (*e.g.*, inflammatory bowel disease, endocrine disorders), but it is unclear if these are dependent on other risk factors. For example, the use of glucocorticoids is an important cause of osteoporosis and fractures according to the research groups of Kanis *et al.*^[1] and van Staa *et al.*^[36]. In contrast, rheumatoid arthritis determines a fracture risk independently of BMD and the use of glucocorticoids^[37].

Immobility is also an important cause of bone loss. A woman immobilized for 1 mo can lose more bone than she would normally lose in 1 or 2 years of the osteoporotic process^[3].

A family history of osteoporosis might be important and there is some evidence for a genetic component to peak bone mass^[38]. Drugs such as corticosteroids and thyroid replacement treatments increase the risk of osteoporosis, as does excessive alcohol consumption^[3]. These risk factors have a dose-dependent effect: The higher the exposure to these substances, the greater the risk (*i.e.*, daily intake of about 3 units)^[1,17].

Fracture risk assessment tool

All postmenopausal women and men 50 years of age and older should be assessed for osteoporosis risk in order to establish the need for BMD measurement and/or vertebral imaging.

Low BMD alone is a poor predictor of fracture in men and women, indicating the need for tools that predict fracture risk independent of, or in addition to, BMD. The use of risk assessment tools that include clinically relevant risk factors to predict fracture risk are being increasingly incorporated into osteoporosis screening and treatment guidelines.

The World Health Organization (WHO) and the International Osteoporosis Foundation advice that fracture risk should be expressed as a short-term absolute risk. The absolute risk of fracture is relative to age and life expectancy as well as the current relative risk, *i.e.*, the probability over a 10-year interval^[1,39]. The period of 10 years comprises the probable duration of treatment and the benefits that might persist once treatment is suspended.

Algorithm that combines the influence of CRFs on fracture risk, integrating or not data on BMD, is FRAX^[8,40,41].

which takes into account the risk factors previously described in Table 1.

The FRAX tool (www.shef.ac.uk/FRAX) calculates alternatively the 10-year probability of hip or major osteoporotic fracture (hip, spine, hip, humerus or forearm fracture). Probabilities can be calculated for the different countries^[40,41]. In all national treatment guidelines some case-finding approach is proposed for patient recognition. However, they differ on the basis of recognized risk factors, BMD and fracture risk assessment. Moreover, recommendations in national guidelines are not always implemented.

According to the Italian guidelines for osteoporosis treatment, postmenopausal women, men, and individuals taking glucocorticoids are included in the program of prevention, screening and diagnosis. Bone densitometry is suggested for all women aged 65 years and over, but, for men and younger postmenopausal women, only for those with CRFs. The guidelines recognize FRAX as a tool for estimating fracture probability and propose that pharmacological treatment should be indicated for people with "rather high" fracture risk but do not identify intervention thresholds^[40].

Assessment of fracture risk: Available imaging methods

Osteoporosis causes loss of bone mass and deterioration of bone microarchitecture with a consequent reduction in bone stiffness and strength, thus resulting in an increased risk of fragility fractures.

Early diagnosis is essential for timely treatment and for identification of patients who are at a higher risk of fractures. Currently, osteoporosis diagnosis and fracture risk assessment are based on the quantitative BMD evaluation realized by the gold standard dual-energy X-ray absorptiometry (DXA). However, BMD assessment (which is a measure of bone mass) only partially provides information about bone strength. Indeed, on one hand BMD is a measure of bone mass, and on the other hand, bone fragility is dependent also on its microarchitecture quality which is determined by all the features (microarchitecture, microdamage and remodeling rates in bone) that influence a bone's ability to resist fracture. The decay of trabecular bone microarchitecture has been acknowledged, among the features, as a major contributor to bone fragility^[42].

Because DXA is a two-dimensional technique, it does have intrinsic limitations; it cannot aid in discriminating cortical from cancellous bone and cannot aid in distinguishing changes due to bone geometry from those due entirely to increased bone density.

There are several recently developed approaches that can provide complementary information for assessing fracture risks in addition to BMD. One of them is the quantitative computed tomography (QCT) which has been developed to assess bone loss^[43]. In QCT trabecular bone can be examined separately from cortical portion of bone and a true value for mineral density is given, unlike other techniques^[3,44].

In addition, currently, the microarchitecture of cancellous bone can be evaluated *in vivo* by high-resolution peripheral QCT techniques. However, such imaging techniques remain a high-end research tool rather than a diagnostic tool for clinical applications^[42].

Other imaging techniques have been developed in order to improve the correct osteoporosis diagnosis, because the accurate diagnosis of osteoporosis leads to a better management in terms of prevention and appropriate pharmacologic or surgical treatment.

It has been demonstrated that BMD evaluations on reference anatomical sites, spine and proximal femur standardly evaluated by DXA examinations, are the most reliable available tool to predict the risk of osteoporotic fractures.

Unfortunately, DXA has precise limitations (*i.e.*, bulky device, high cost, limited accessibility and use of ionizing radiation) that impede its application for population screenings and primary care diagnosis.

These limits have resulted in the development of an increasing number of radiation-free United States-based technologies as screening tools for early osteoporosis diagnosis and fracture prevention^[45-48].

However, the actual clinical utility of United States devices for osteoporosis diagnosis is quite limited since they are referred only to peripheral sites (*i.e.*, calcaneus, radius, tibia, *etc.*).

To overcome this limitation, a novel ultrasound approach has recently been developed to evaluate bone status and fragility fracture risk^[49,50]. In this context, this new ultrasonic method is the first tool for bone characterization and microarchitecture assessment that enables the scanning of central axial reference sites (lumbar vertebrae and proximal femur) through an innovative approach without the use of ionizing radiations.

Unfortunately, in many countries, even patients at high risk of fractures might not be able to obtain therapy because effectual medicines are not reimbursed by government health insurance plans^[10]. Moreover, worldwide osteoporosis is under-diagnosed, under-recognized and undertreated, and only a small number of patients with fractures receives proper investigation and therapy.

In 1994, a statement on the evaluation of fracture risk and its usage in screening for postmenopausal osteoporosis has been published by the WHO. In this report diagnostic criteria for BMD measurement have been provided and osteoporosis has been described as a recognized and well-defined disease that affected more than 75 million people in the world^[3]. Based on WHO recommendations, national guidelines have been developed for osteoporosis management focusing mainly on the prevention of fractures in postmenopausal women.

In recent years, integrated programs to improve the management of osteoporosis are under development in some countries. Among the various aspects considered in these programs, those of particular relevance are related to education, improved screening and treatment efficacy monitoring. Indeed, many studies show that these

programs reduce the risk of hip fractures compared to standard management^[40]. Then, osteoporotic fractures are preventable by implementation of programs to assess and treat high risk individuals.

Geographical factors

Substantial difference has been shown in hip fracture incidence rates around the world due to environmental factors and lifestyle or cultural differences^[8,51]. Generally the incidence of hip fracture increases with age. Moreover, the incidence rate differs across different regions or ethnic groups^[30]. In Scandinavia and in North America, age-adjusted rates seem to be highest with almost seven-fold lower rates in Southern Europe^[51,52]. The incidence of hip fracture is also lower in Asia, Latin America and Africa^[53,54], particularly in rural areas^[55-57].

In fact, bone mass is lower in Norwegian and Swedish with respect to other European people^[58]. Whereas, Chinese, Japanese, South Koreans and black Africans show significantly lower bone mineral content (BMC) with respect to Western Caucasian populations^[59-61]. One probable reason for this evidence is the difference between studies leading to different levels of underreporting^[30]. Furthermore, compared to Caucasian, African Americans have a higher BMC, but likewise a lower prevalence of osteoporosis^[30]. The lower hip fracture incidence rates among Asians and blacks can be due to also to their shorter hip axis length^[62]. The genetic background of populations in the studied regions is an important factor to explain global variations in hip fractures. For example, the hip fracture incidence rates in Ontario are similar to those in the United Kingdom because older cohorts in Ontario are of English ancestry^[63]. Likewise, incidence rates are similar in Mexico and Spain; in fact, this two population group share the same genetic background^[64]. Rates in Argentina are close to those from other predominantly populations because the ethnic background in Argentina is largely Caucasian. Furthermore, many Scandinavian cities where immigration is increasing have lower hip fracture rates than those with uniformly Scandinavian populations^[65].

The worldwide risk of hip fracture is variable more in women than in men. Women have a higher osteoporosis risk; in the United States the lifetime risk of a hip fracture from age 50 years onward has been estimated at 17% and only 6% for Caucasian women and men, respectively. Among Asian, black, and Hispanic population, women and men were about 50% and 40% less susceptible to fracture with respect to white women and white men, respectively^[66]. The rates in men and women are similar in low risk populations, particularly those of Asian or African heritage^[30].

The incidence rate of hip fractures depends also on the country's development. Where life expectancy at birth is low and the population is very young, as well as in African countries, the hip fracture incidence rates are the lowest^[67,68]. However, the low incidence might be an artifact due to incomplete case ascertainment or national

health database unavailability in developing countries.

The improvement of health care and the augmented life expectancy due to industrialization and urbanization have led to an increased incidence of hip fracture^[30]. In fact, the rapid modernization and the consequent decline in routine load of physical activity induced an increased fracture incidence of the hip in Hong Kong^[69] and Beijing^[70]. Moreover urban settings have higher incidence rates than rural ones (*i.e.*, Oslo, Norway)^[56,71,72].

PREVALENCE OF OSTEOPOROTIC FRACTURE

Between 1990 and 2000, osteoporosis caused a 25% worldwide increment in hip fractures. The peak for hip or other fracture types occurs for both women and men aged 75-79 years and 50-59 years, respectively^[73]. The annual number of hip fractures will grow significantly with the sustained ageing of the people. It is estimated that this demographic trend could induce a global increment of hip fractures from about 2 million in 1990 to a projected 6 million in 2050^[9,10]. However, the future worldwide load of age-related fractures (hip and others) should be predicted by analyzing the variations in fracture incidence rates adjusted for demographic changes in the global population. Assuming a 1% annual rise in incidence adjusted for age, hip fractures in 2050 could exceed 8 million; if rates stabilized in Europe and North America but rose by 3% per year in the rest of the world, the total could account for more than 21 million^[10,11] (Figure 1).

By 2050, the global incidence of hip fracture is expected to increase more than 300% and 240% in men and in women, respectively^[11]. In women aged 45 years or more, the number of days spent in the hospital due to osteoporosis are greater than those due to other pathologies, such as breast cancer, diabetes, and myocardial infarction^[74]. In Switzerland hospital bed days related to osteoporotic fracture are higher than those related to stroke and other cardiac disease^[75]. In England, a fifth of all orthopedic beds are dedicated to hip fractures^[10] and the cost related to osteoporotic fractures treatment in postmenopausal women has been estimated to reach about 2 billion dollars or more by 2020^[76]. In Spain, there are around 2 million osteoporotic women (about 30% of them are aged 50 years or more): Each year 25000 fractures arise and cause, consequently, direct costs of about €120 million and indirect costs of about €400 million^[77]. In Italy, approximately 4 million of women and 800 thousand men are thought to be affected by osteoporosis. In 1998, the European Commission estimated an incidence rise of hip fractures from 117000 to 240000 in the year 2000 in Germany^[78]. However, the highest risk of hip fractures are shown in Northern Europe and the United States^[79]. In Swedish male population the number of hospital bed days related to osteoporotic fractures are higher than those related to prostate cancer^[80]. In Denmark, in

population group aged 50 years or more, about 40% of women and 20% of men are osteoporotic^[81]. In Finland, hip fractures total number augmented by 70% within a 10-year period (1992-2002)^[82].

In the United States, among people aged 50 years or more, there were approximately 12 million cases of osteoporosis in 2010; this data are estimated to increase up to 14 million cases of disease by 2020^[83], inducing the number of hip fractures to triple by 2040^[84]. In Canada, osteoporosis affects 1.4 million postmenopausal women and the elderly. Almost 30000 hip fractures occur each year, and approximately 80% of these fractures are related to osteoporosis^[85]. By the year 2030, the cases of hip fractures is estimated to quadruple^[86].

In Australia, osteoporosis affects 2.2 million people (approximately 11% of men and 27% of women aged 60 years or more), causing 20000 hip fractures per year (growing by 40% every ten years), with total disease-related costs of \$7.4 billion per year (\$1.9 billion of direct costs)^[87].

It is expected that approximately half of all osteoporotic hip fractures will take place in Asia by the year 2050^[11]. Osteoporosis affects almost 70 million Chinese aged 50 years or more causing 687000 hip fractures each year^[88]. In Japan, hip fractures total number was 153000 in 2010 and is projected to be 238000 in 2030^[89].

Economic burden

In Europe, the total osteoporosis economic burden was estimated at €30.7 billion in 2010. The increment of direct costs is expected to be due to changes in demography to 76.7 billion in 2050^[73]. In the United States, the medical cost of osteoporosis and related fractures is estimated at \$20 billion per year^[10], and can be predicted to be at \$50 in 2050 due to the annual increase in incidence of osteoporotic fractures adjusted for age. China spent approximately \$1.5 billion treating hip fracture in 2006. It is projected that this will grow to \$12.5 billion in 2020 and to more than \$264.7 billion by 2050^[90] (Figure 2).

The WHO considers osteoporosis to be second only to cardiovascular diseases as a crucial health problem^[74]. The disability caused by osteoporosis is comparable or even greater than that produced by cancers and by different chronic non-transmissible pathologies, as reported by Johnell and Kanis^[73] in 2006. Furthermore, the total costs per year of osteoporosis exceeds those for a variety of brain disorders^[91] (Figure 3).

Currently in Europe, the annual expenditure for osteoporosis corresponds about to 3.5% of the total spent on health care^[40]. However, osteoporosis total cost in a country is difficult to estimate because it depends on various factors, such as fracture risk related to age, size of population, acute hospital care, cost per fracture, long-term care at home, needs of nursing home care after hip fracture occurrence, medications, rehabilitation, treatment and loss of working days. Sometimes estimated costs are based on many assumptions that are

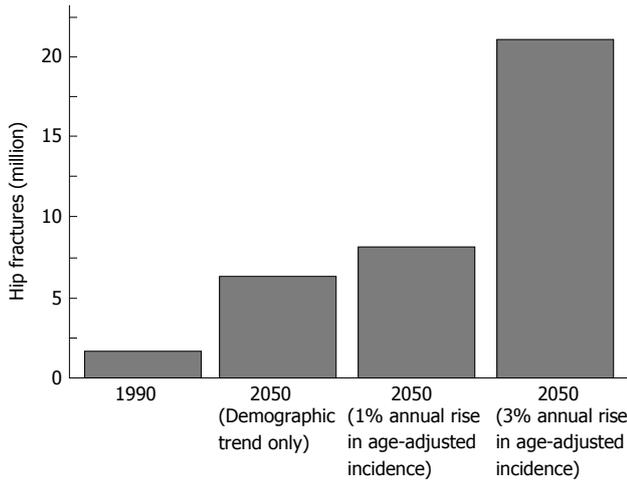


Figure 1 Hip fractures expected impact. Incidence of hip fractures worldwide adjusted for demographic changes.

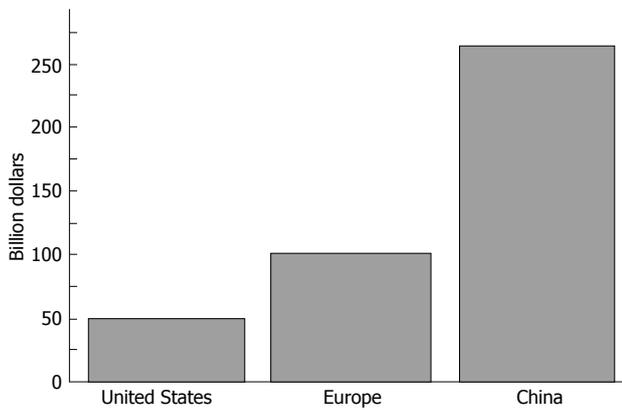


Figure 2 Economic burden. Expected costs in 2050 based on changes in demography.

difficult to test. Moreover, not all costs related to fracture come from a country's healthcare budget (e.g., long-term care, community care).

Generally, a greater part of costs is related to incident fractures, whereas pharmacological treatment only represents less than 5% of total costs. The monetary burden depends mainly on the fracture risk; in fact, the cost per fracture increases with age (the 70% of the total costs are related to people aged more than 70 years). Also, fractures occurred in women represent the main part of the total cost^[40].

Hip fractures account for more than half of the cost, whereas that of vertebral fractures is underestimated because of the difficulties of studying them. Only few people with clinical vertebral fractures become hospitalized^[92] and, therefore, these cases are more complex to include in observational studies^[93].

Outcome of osteoporotic fracture

Osteoporosis load is referred not only to fractures, costs, mortality, morbidity, but also to quality-adjusted life years (QALYs) lost.

Generally osteoporotic fractures caused more deaths

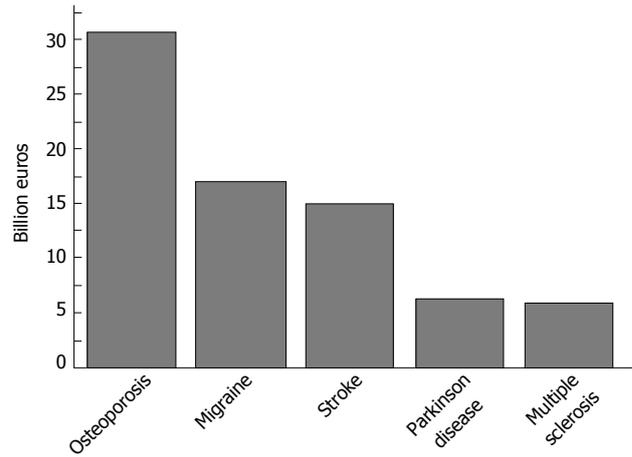


Figure 3 Total cost of osteoporosis vs brain disorders.

and morbidity than cancer (except lung cancer). In particular, fracture of the hip is responsible for more deaths than suicide and transportation accidents^[40].

The fractures effect on survival is related to the fracture type^[94]. Hip fractures are the most dangerous, since approximately 10%-20% women with hip fractures die than expected for age within the first year. Moreover, the mortality is greater for men, and the death risk is greatest immediately after the fracture and decreases over time^[10], even if it seems that mortality rates after fracture of hip have remained constant over the past 20 years^[95]. Very often osteoporosis related fractures cause loss of physical functioning including loss of mobility and self-care. Approximately 7% of women become dependent on others to assist with the basic activities of daily living, and an additional 8% require nursing home care. The main long-term damage is in the capability to walk; half of patients able to walk before fracture cannot do so autonomously afterwards. Furthermore, up to a third of individuals who have a fracture of the hip can become totally dependent^[96].

The principal vertebral fractures consequences are height loss, kyphosis, and back pain. Compression fractures cause acute symptoms^[97] but many fractures seem to occur without pain. Women with vertebral deformities are substantially more likely to have chronic back pain as well as future fractures. Vertebral fractures, however, affect not only physical function but also physical aspect, and humor^[10].

Osteoporosis load can also be quantified by loss of quality of life (QoL). Loss of QoL reflects the disutility or loss in utility due to both the pathology and increased mortality. The utility loss caused by fracture depend on the site of fracture; in fact, fractures of the axial anatomic sites (hip and vertebrae) induce more disutility with respect to forearm fractures. The loss of utility is similar for the both sexes^[98]. During the first year after fracture of hip, vertebrae and wrist a person's utility (relative to the age-specific utility) has been estimated to be 0.70, 0.59 and 0.96, respectively. On the other hand, in the subsequent years quality of life was assumed to be 80% of that of a healthy individual^[99].

Combining mortality and loss of QoL, it is possible to evaluate the annual number of lost QALYs due to fractures. It is estimated that Germany has the highest number of lost QALYs due to its high fracture incidence and its great population. The estimation of QALYs lost due to fracture-related deaths was done considering an averaged interval time of four months between fracture and death^[82]. Mortality during the first year after fractures represents approximately 1% and 3% of the total QALY-loss in women and men, respectively. A great part of the QALYs lost derives from the long-term disability after fractures due to osteoporosis. This component is larger in women, because men have a higher absolute mortality after fracture.

CONCLUSION

Osteoporosis incidence is rising in many countries. Osteoporotic fractures are a crucial public health concern and represent one of the main and frequent cause of disability and medical costs worldwide. Therefore, early diagnosis of patients with high risk of osteoporotic fractures is essential. Fortunately osteoporotic fractures are preventable. The comprehension of the main factors causing this "silent disease" could help the prediction of fractures in high-risk individuals worldwide. Early diagnosis of a larger range of the population is the key to resizing the impact of osteoporosis on the health-care system. With this, it is necessary to encourage the widespread use of quick, cheap, non-invasive screening techniques and to increase national awareness campaigns promoting a healthy lifestyle across countries.

REFERENCES

- Kanis JA**, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int* 2013; **24**: 23-57 [PMID: 23079689 DOI: 10.1007/s00198-012-2074-y]
- Albright F**. Annals of internal medicine, Volume 27, 1947: Osteoporosis. *Nutr Rev* 1989; **47**: 85-86 [PMID: 2649807]
- World Health Organization**. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. *World Health Organ Tech Rep Ser* 1994; **843**: 1-129 [PMID: 7941614]
- Anil G**, Guglielmi G, Peh WC. Radiology of osteoporosis. *Radiol Clin North Am* 2010; **48**: 497-518 [PMID: 20609888 DOI: 10.1016/j.rcl.2010.02.016]
- Guglielmi G**, Muscarella S, Leone A, Peh WC. Imaging of metabolic bone diseases. *Radiol Clin North Am* 2008; **46**: 735-754, vi [PMID: 18922290 DOI: 10.1016/j.rcl.2008.04.010]
- NOF**. Fast facts. 2008. Available from: URL: <http://www.nof.org/aboutosteoporosis>
- Willson T**, Nelson SD, Newbold J, Nelson RE, LaFleur J. The clinical epidemiology of male osteoporosis: a review of the recent literature. *Clin Epidemiol* 2015; **7**: 65-76 [PMID: 25657593 DOI: 10.2147/CLEP.S40966]
- Giusti A**, Bianchi G. Male osteoporosis. *Reumatismo* 2014; **66**: 136-143 [PMID: 25069495 DOI: 10.4081/reumatismo.2014.786]
- Cooper C**, Campion C, Melton LJ. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int* 1992; **2**: 285-289 [PMID: 1421796]
- Cummings SR**, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002; **359**: 1761-1767 [PMID: 12049882]
- Gullberg B**, Johnell O, Kanis JA. World-wide projections for hip fracture. *Osteoporos Int* 1997; **7**: 407-413 [PMID: 9425497 DOI: 10.1007/PL00004148]
- Kanis JA**, Black D, Cooper C, Dargent P, Dawson-Hughes B, De Laet C, Delmas P, Eisman J, Johnell O, Jonsson B, Melton L, Oden A, Papapoulos S, Pols H, Rizzoli R, Silman A, Tenenhouse A. A new approach to the development of assessment guidelines for osteoporosis. *Osteoporos Int* 2002; **13**: 527-536 [PMID: 12111012 DOI: 10.1007/s001980200069]
- Cosman F**, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int* 2014; **25**: 2359-2381 [PMID: 25182228 DOI: 10.1007/s00198-014-2794-2]
- Riggs BL**, Melton LJ. Involutional osteoporosis. *N Engl J Med* 1986; **314**: 1676-1686 [PMID: 3520321 DOI: 10.1056/NEJM198606263142605]
- Mazess RB**, Barden HS. Bone densitometry for diagnosis and monitoring osteoporosis. *Proc Soc Exp Biol Med* 1989; **191**: 261-271 [PMID: 2662200]
- De Laet C**, Kanis JA, Odén A, Johanson H, Johnell O, Delmas P, Eisman JA, Kroger H, Fujiwara S, Garnero P, McCloskey EV, Mellstrom D, Melton LJ, Meunier PJ, Pols HA, Reeve J, Silman A, Tenenhouse A. Body mass index as a predictor of fracture risk: a meta-analysis. *Osteoporos Int* 2005; **16**: 1330-1338 [PMID: 15928804 DOI: 10.1007/s00198-005-1863-y]
- Kanis JA**, Borgstrom F, De Laet C, Johansson H, Johnell O, Jonsson B, Oden A, Zethraeus N, Pflieger B, Khaltayev N. Assessment of fracture risk. *Osteoporos Int* 2005; **16**: 581-589 [PMID: 15616758]
- Johnell O**, Kanis JA, Oden A, Johansson H, De Laet C, Delmas P, Eisman JA, Fujiwara S, Kroger H, Mellstrom D, Meunier PJ, Melton LJ, O'Neill T, Pols H, Reeve J, Silman A, Tenenhouse A. Predictive value of BMD for hip and other fractures. *J Bone Miner Res* 2005; **20**: 1185-1194 [PMID: 15940371]
- Klotzbuecher CM**, Ross PD, Landsman PB, Abbott TA, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 2000; **15**: 721-739 [PMID: 10780864 DOI: 10.1359/jbmr.2000.15.4.721]
- Kanis JA**, Johansson H, Oden A, Johnell O, De Laet C, Eisman JA, McCloskey EV, Mellstrom D, Melton LJ, Pols HA, Reeve J, Silman AJ, Tenenhouse A. A family history of fracture and fracture risk: a meta-analysis. *Bone* 2004; **35**: 1029-1037 [PMID: 15542027 DOI: 10.1016/j.bone.2004.06.017]
- Svejme O**, Ahlborg HG, Nilsson JÅ, Karlsson MK. Low BMD is an independent predictor of fracture and early menopause of mortality in post-menopausal women—a 34-year prospective study. *Maturitas* 2013; **74**: 341-345 [PMID: 23374709]
- Davies MC**, Hall ML, Jacobs HS. Bone mineral loss in young women with amenorrhoea. *BMJ* 1990; **301**: 790-793 [PMID: 2224267 DOI: 10.1136/bmj.301.6755.790]
- Prior JC**, Vigna YM, Schechter MT, Burgess AE. Spinal bone loss and ovulatory disturbances. *N Engl J Med* 1990; **323**: 1221-1227 [PMID: 2215605 DOI: 10.1056/NEJM199011013231801]
- Finkelstein JS**, Klibanski A, Neer RM, Greenspan SL, Rosenthal DI, Crowley WF. Osteoporosis in men with idiopathic hypogonadotropic hypogonadism. *Ann Intern Med* 1987; **106**: 354-361 [PMID: 3544993]
- Seeman E**, Melton LJ, O'Fallon WM, Riggs BL. Risk factors for spinal osteoporosis in men. *Am J Med* 1983; **75**: 977-983 [PMID: 6650552 DOI: 10.1016/0002-9343(83)90878-1]
- Baron JA**. Smoking and estrogen-related disease. *Am J Epidemiol* 1984; **119**: 9-22 [PMID: 6362403]
- Hofbauer LC**, Khosla S, Dunstan CR, Lacey DL, Spelsberg TC, Riggs BL. Estrogen stimulates gene expression and protein production of osteoprotegerin in human osteoblastic cells. *Endocrinology* 1999; **140**: 4367-4370 [PMID: 10465311 DOI: 10.1210/endo.140.9.7131]

- 28 **Saika M**, Inoue D, Kido S, Matsumoto T. 17beta-estradiol stimulates expression of osteoprotegerin by a mouse stromal cell line, ST-2, via estrogen receptor-alpha. *Endocrinology* 2001; **142**: 2205-2212 [PMID: 11356664 DOI: 10.1210/endo.142.6.8220]
- 29 **Khosla S**, Melton LJ, Atkinson EJ, O'Fallon WM, Klee GG, Riggs BL. Relationship of serum sex steroid levels and bone turnover markers with bone mineral density in men and women: a key role for bioavailable estrogen. *J Clin Endocrinol Metab* 1998; **83**: 2266-2274 [PMID: 9661593 DOI: 10.1210/jcem.83.7.4924]
- 30 **Cheng SY**, Levy AR, Lefavre KA, Guy P, Kuramoto L, Sobolev B. Geographic trends in incidence of hip fractures: a comprehensive literature review. *Osteoporos Int* 2011; **22**: 2575-2586 [PMID: 21484361 DOI: 10.1007/s00198-011-1596-z]
- 31 **Lips P**. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev* 2001; **22**: 477-501 [PMID: 11493580 DOI: 10.1210/edrv.22.4.0437]
- 32 **Compston J**. Clinical and therapeutic aspects of osteoporosis. *Eur J Radiol* 2009; **71**: 388-391 [PMID: 19660883 DOI: 10.1016/j.ejrad.2008.04.063]
- 33 **Guglielmi G**, Muscarella S, Bazzocchi A. Integrated imaging approach to osteoporosis: state-of-the-art review and update. *Radiographics* 2011; **31**: 1343-1364 [PMID: 21918048 DOI: 10.1148/rq.315105712]
- 34 **Evans JG**, Seagroatt V, Goldacre MJ. Secular trends in proximal femoral fracture, Oxford record linkage study area and England 1968-86. *J Epidemiol Community Health* 1997; **51**: 424-429 [PMID: 9328551 DOI: 10.1136/jech.51.4.424]
- 35 **Cooper C**, Eriksson JG, Forsén T, Osmond C, Tuomilehto J, Barker DJ. Maternal height, childhood growth and risk of hip fracture in later life: a longitudinal study. *Osteoporos Int* 2001; **12**: 623-629 [PMID: 11580075]
- 36 **van Staa TP**, Leufkens HG, Cooper C. The epidemiology of corticosteroid-induced osteoporosis: a meta-analysis. *Osteoporos Int* 2002; **13**: 777-787 [PMID: 12378366 DOI: 10.1007/s001980200108]
- 37 **Kanis JA**, Johansson H, Oden A, Johnell O, de Laet C, Melton III LJ, Tenenhouse A, Reeve J, Silman AJ, Pols HA, Eisman JA, McCloskey EV, Mellstrom D. A meta-analysis of prior corticosteroid use and fracture risk. *J Bone Miner Res* 2004; **19**: 893-899 [PMID: 15125788 DOI: 10.1359/JBMR.040134]
- 38 **Slemenda CW**, Christian JC, Williams CJ, Norton JA, Johnston CC. Genetic determinants of bone mass in adult women: a reevaluation of the twin model and the potential importance of gene interaction on heritability estimates. *J Bone Miner Res* 1991; **6**: 561-567 [PMID: 1887818 DOI: 10.1002/jbmr.5650060606]
- 39 **Kanis JA**, Johnell O, Oden A, De Laet C, Jonsson B, Dawson A. Ten-year risk of osteoporotic fracture and the effect of risk factors on screening strategies. *Bone* 2002; **30**: 251-258 [PMID: 11792594 DOI: 10.1016/S8756-3282(01)00653-6]
- 40 **Ström O**, Borgström F, Kanis JA, Compston J, Cooper C, McCloskey EV, Jönsson B. Osteoporosis: burden, health care provision and opportunities in the EU: a report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos* 2011; **6**: 59-155 [PMID: 22886101 DOI: 10.1007/s11657-011-0060-1]
- 41 **Kanis JA**, Oden A, Johnell O, Johansson H, De Laet C, Brown J, Burckhardt P, Cooper C, Christiansen C, Cummings S, Eisman JA, Fujiwara S, Glüer C, Goltzman D, Hans D, Krieg MA, La Croix A, McCloskey E, Mellstrom D, Melton LJ, Pols H, Reeve J, Sanders K, Schott AM, Silman A, Torgerson D, van Staa T, Watts NB, Yoshimura N. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int* 2007; **18**: 1033-1046 [PMID: 17323110 DOI: 10.1007/s00198-007-0343-y]
- 42 **Dong X**, Wang X. Assessment of bone fragility with clinical imaging modalities. *Hard Tissue* 2013; **2**: 7 [PMID: 24294491 DOI: 10.13172/2050-2303-2-1-351]
- 43 **Adams JE**. Radiogrammetry and radiographic absorptiometry. *Radiol Clin North Am* 2010; **48**: 531-540 [PMID: 20609890 DOI: 10.1016/j.rcl.2010.03.006]
- 44 **Guglielmi G**, Lang TF. Quantitative computed tomography. *Semin Musculoskelet Radiol* 2002; **6**: 219-227 [PMID: 12541199 DOI: 10.1055/s-2002-36719]
- 45 **Pais R**, Campean R, Simon S, Bolosiu CR, Muntean L, Bolosiu HD. Accuracy of Quantitative Ultrasound Parameters in the Diagnosis of Osteoporosis. *Cent Eur J Med* 2010; **5**: e478-e485 [DOI: 10.2478/s11536-009-0076-8]
- 46 **Laugier P**. Quantitative ultrasound of bone: looking ahead. *Joint Bone Spine* 2006; **73**: 125-128 [PMID: 16488646 DOI: 10.1016/j.jbspin.2005.10.012]
- 47 **Holi MS**, Radhakrishnan S, Swaranamani S, Ayavelan NA. Quantitative ultrasound technique for the assessment of osteoporosis and prediction of fracture risk. *J Pure Appl Ultrason* 2005; **27**: e55-e60
- 48 **Khaw KT**, Reeve J, Luben R, Bingham S, Welch A, Wareham N, Oakes S, Day N. Prediction of total and hip fracture risk in men and women by quantitative ultrasound of the calcaneus: EPIC-Norfolk prospective population study. *Lancet* 2004; **363**: 197-202 [PMID: 14738792 DOI: 10.1016/S0140-6736(03)15325-1]
- 49 **Conversano F**, Franchini R, Greco A, Soloperto G, Chiriaco F, Casciaro E, Aventaggiato M, Renna MD, Pisani P, Di Paola M, Grimaldi A, Quarta L, Quarta E, Muratore M, Laugier P, Casciaro S. A novel ultrasound methodology for estimating spine mineral density. *Ultrasound Med Biol* 2015; **41**: 281-300 [PMID: 25438845 DOI: 10.1016/j.ultrasmedbio.2014.08.017]
- 50 **Pisani P**, Greco A, Renna MD, Conversano F, Casciaro E, Quarta L, Costanza D, Muratore M, Casciaro S. An Innovative Ultrasound-Based Method for The Identification of Patients at High Fracture Risk. Proceedings of the 3rd Imeko TC13 Symposium on Measurements in Biology and Medicine. New Frontiers in Biomedical Measurements, 2014: e50-e53
- 51 **Cooper C**, Cole ZA, Holroyd CR, Earl SC, Harvey NC, Dennison EM, Melton LJ, Cummings SR, Kanis JA. Secular trends in the incidence of hip and other osteoporotic fractures. *Osteoporos Int* 2011; **22**: 1277-1288 [PMID: 21461721 DOI: 10.1007/s00198-011-1601-6]
- 52 **Johnell O**, Gullberg B, Allander E, Kanis JA. The apparent incidence of hip fracture in Europe: a study of national register sources. *Osteoporos Int* 1992; **2**: 298-302 [PMID: 1421798 DOI: 10.1007/BF01623186]
- 53 **Yan L**, Zhou B, Prentice A, Wang X, Golden MH. Epidemiological study of hip fracture in Shenyang, People's Republic of China. *Bone* 1999; **24**: 151-155 [PMID: 9951786 DOI: 10.1016/S8756-3282(98)00168-9]
- 54 **Morales-Torres J**, Gutiérrez-Ureña S. The burden of osteoporosis in Latin America. *Osteoporos Int* 2004; **15**: 625-632 [PMID: 15292978 DOI: 10.1007/s00198-004-1596-3]
- 55 **Kaastad TS**, Meyer HE, Falch JA. Incidence of hip fracture in Oslo, Norway: differences within the city. *Bone* 1998; **22**: 175-178 [PMID: 9477241 DOI: 10.1016/S8756-3282(97)00247-0]
- 56 **Sanders KM**, Nicholson GC, Ugoni AM, Seeman E, Pasco JA, Kotowicz MA. Fracture rates lower in rural than urban communities: the Geelong Osteoporosis Study. *J Epidemiol Community Health* 2002; **56**: 466-470 [PMID: 12011207 DOI: 10.1136/jech.56.6.466]
- 57 **Cooper C**. Epidemiology of Osteoporosis. *Osteoporos Int* 1999; **2**: eS2-eS8 [DOI: 10.1007/PL00004156]
- 58 **Lunt M**, Felsenberg D, Adams J, Benevolenskaya L, Cannata J, Dequeker J, Dodenhof C, Falch JA, Johnell O, Khaw KT, Masaryk P, Pols H, Poor G, Reid D, Scheidt-Nave C, Weber K, Silman AJ, Reeve J. Population-based geographic variations in DXA bone density in Europe: the EVOS Study. European Vertebral Osteoporosis. *Osteoporos Int* 1997; **7**: 175-189 [PMID: 9205628 DOI: 10.1007/BF01622286]
- 59 **Cundy T**, Cornish J, Evans MC, Gamble G, Stapleton J, Reid IR. Sources of interracial variation in bone mineral density. *J Bone Miner Res* 1995; **10**: 368-373 [PMID: 7785457 DOI: 10.1002/jbmr.5650100306]
- 60 **Russell-Aulet M**, Wang J, Thornton JC, Colt EW, Pierson RN.

- Bone mineral density and mass in a cross-sectional study of white and Asian women. *J Bone Miner Res* 1993; **8**: 575-582 [PMID: 8511984 DOI: 10.1002/jbmr.5650080508]
- 61 **Aspray TJ**, Prentice A, Cole TJ, Sawo Y, Reeve J, Francis RM. Low bone mineral content is common but osteoporotic fractures are rare in elderly rural Gambian women. *J Bone Miner Res* 1996; **11**: 1019-1025 [PMID: 8797124 DOI: 10.1002/jbmr.5650110720]
- 62 **Cummings SR**, Cauley JA, Palermo L, Ross PD, Wasnich RD, Black D, Faulkner KG. Racial differences in hip axis lengths might explain racial differences in rates of hip fracture. Study of Osteoporotic Fractures Research Group. *Osteoporos Int* 1994; **4**: 226-229 [PMID: 7949753 DOI: 10.1007/BF01623243]
- 63 **Jaglal SB**, Sherry PG, Schatzker J. The impact and consequences of hip fracture in Ontario. *Can J Surg* 1996; **39**: 105-111 [PMID: 8769920]
- 64 **Clark P**, Lavielle P, Franco-Marina F, Ramírez E, Salmerón J, Kanis JA, Cummings SR. Incidence rates and life-time risk of hip fractures in Mexicans over 50 years of age: a population-based study. *Osteoporos Int* 2005; **16**: 2025-2030 [PMID: 16133641 DOI: 10.1007/s00198-005-1991-4]
- 65 **Rogmark C**, Sernbo I, Johnell O, Nilsson JA. Incidence of hip fractures in Malmö, Sweden, 1992-1995. A trend-break. *Acta Orthop Scand* 1999; **70**: 19-22 [PMID: 10191741 DOI: 10.3109/17453679909000950]
- 66 **Tosteson AN**, Melton LJ, Dawson-Hughes B, Baim S, Favus MJ, Khosla S, Lindsay RL. Cost-effective osteoporosis treatment thresholds: the United States perspective. *Osteoporos Int* 2008; **19**: 437-447 [PMID: 18292976 DOI: 10.1007/s00198-007-0550-6]
- 67 **El Maghraoui A**, Koumba BA, Jroundi I, Achemlal L, Bezza A, Tazi MA. Epidemiology of hip fractures in 2002 in Rabat, Morocco. *Osteoporos Int* 2005; **16**: 597-602 [PMID: 15452688 DOI: 10.1007/s00198-004-1729-8]
- 68 **Zebaze RM**, Seeman E. Epidemiology of hip and wrist fractures in Cameroon, Africa. *Osteoporos Int* 2003; **14**: 301-305 [PMID: 12730790 DOI: 10.1007/s00198-002-1356-1]
- 69 **Lau EM**, Cooper C. The epidemiology of osteoporosis. The oriental perspective in a world context. *Clin Orthop Relat Res* 1996; (**323**): 65-74 [PMID: 8625608 DOI: 10.1097/00003086-199602000-00009]
- 70 **Xu L**, Haworth IS, Kulkarni AA, Bolger MB, Davies DL. Mutagenesis and cysteine scanning of transmembrane domain 10 of the human dipeptide transporter. *Pharm Res* 2009; **26**: 2358-2366 [PMID: 19685173 DOI: 10.1007/s11095-009-9952-9]
- 71 **Chevalley T**, Herrmann FR, Delmi M, Stern R, Hoffmeyer P, Rapin CH, Rizzoli R. Evaluation of the age-adjusted incidence of hip fractures between urban and rural areas: the difference is not related to the prevalence of institutions for the elderly. *Osteoporos Int* 2002; **13**: 113-118 [PMID: 11905521 DOI: 10.1007/s001980200002]
- 72 **Bjørgul K**, Reikerås O. Incidence of hip fracture in southeastern Norway: a study of 1,730 cervical and trochanteric fractures. *Int Orthop* 2007; **31**: 665-669 [PMID: 17033761 DOI: 10.1007/s00264-006-0251-3]
- 73 **Johnell O**, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int* 2006; **17**: 1726-1733 [PMID: 16983459]
- 74 **Kanis JA**, Delmas P, Burckhardt P, Cooper C, Torgerson D. Guidelines for diagnosis and management of osteoporosis. The European Foundation for Osteoporosis and Bone Disease. *Osteoporos Int* 1997; **7**: 390-406 [PMID: 9373575 DOI: 10.1007/BF01623782]
- 75 **Lippuner K**, von Overbeck J, Perrelet R, Bosshard H, Jaeger P. Incidence and direct medical costs of hospitalizations due to osteoporotic fractures in Switzerland. *Osteoporos Int* 1997; **7**: 414-425 [PMID: 9425498 DOI: 10.1007/PL00004149]
- 76 **Burge RT**. The cost of osteoporotic fractures in the UK: Projections for 2000-2020. *J Med Econ* 2001; (**4**): e51-e62 [DOI: 10.3111/200104051062]
- 77 **Díaz Curriel M**, García JJ, Carrasco JL, Honorato J, Pérez Cano R, Rapado A, Alvarez Sanz C. [Prevalence of osteoporosis assessed by densitometry in the Spanish female population]. *Med Clin (Barc)* 2001; **116**: 86-88 [PMID: 11181284]
- 78 **Häussler B**, Gothe H, Göl D, Glaeske G, Pientka L, Felsenberg D. Epidemiology, treatment and costs of osteoporosis in Germany—the BoneEVA Study. *Osteoporos Int* 2007; **18**: 77-84 [PMID: 17048064 DOI: 10.1007/s00198-006-0206-y]
- 79 **Kanis JA**, Johnell O, De Laet C, Jonsson B, Oden A, Ogelsby AK. International variations in hip fracture probabilities: implications for risk assessment. *J Bone Miner Res* 2002; **17**: 1237-1244 [PMID: 12096837 DOI: 10.1359/jbmr.2002.17.7.1237]
- 80 **Kanis JA**, Johnell O, Oden A, De Laet C, Mellstrom D. Epidemiology of osteoporosis and fracture in men. *Calcif Tissue Int* 2004; **75**: 90-99 [PMID: 15185058 DOI: 10.1007/s00223-004-0287-6]
- 81 **Vestergaard P**, Rejnmark L, Mosekilde L. Osteoporosis is markedly underdiagnosed: a nationwide study from Denmark. *Osteoporos Int* 2005; **16**: 134-141 [PMID: 15197546 DOI: 10.1007/s00198-004-1680-8]
- 82 **Borgström F**, Sobocki P, Ström O, Jönsson B. The societal burden of osteoporosis in Sweden. *Bone* 2007; **40**: 1602-1609 [PMID: 17433804]
- 83 **National Osteoporosis Foundation**. America's bone health: the state of osteoporosis and low bone mass in our nation. Washington, DC: National Osteoporosis Foundation, 2002
- 84 **Schneider EL**, Guralnik JM. The aging of America. Impact on health care costs. *JAMA* 1990; **263**: 2335-2340 [PMID: 2109105 DOI: 10.1001/jama.1990.03440170057036]
- 85 **Melton LJ**, Thamer M, Ray NF, Chan JK, Chesnut CH, Einhorn TA, Johnston CC, Raisz LG, Silverman SL, Siris ES. Fractures attributable to osteoporosis: report from the National Osteoporosis Foundation. *J Bone Miner Res* 1997; **12**: 16-23 [PMID: 9240721 DOI: 10.1359/jbmr.1997.12.1.16]
- 86 **Jackson SA**, Tenenhouse A, Robertson L. Vertebral fracture definition from population-based data: preliminary results from the Canadian Multicenter Osteoporosis Study (CaMos). *Osteoporos Int* 2000; **11**: 680-687 [PMID: 11095171 DOI: 10.1007/s001980070066]
- 87 **Sambrook PN**, Seeman E, Phillips SR, Ebeling PR. Preventing osteoporosis: outcomes of the Australian Fracture Prevention Summit. *Med J Aust* 2002; **176** Suppl: S1-16 [PMID: 12049064]
- 88 **China Health Promotion Foundation**. Osteoporosis a Summary Statement of China. White Paper China, 2008
- 89 **Hagino H**, Katagiri H, Okano T, Yamamoto K, Teshima R. Increasing incidence of hip fracture in Tottori Prefecture, Japan: trend from 1986 to 2001. *Osteoporos Int* 2005; **16**: 1963-1968 [PMID: 16133645]
- 90 **Luo L**, Xu L. Analysis of direct economic burden of osteoporotic hip fracture and its influence factors. *Chin J Epidemiol* 2005; **9**: 9
- 91 **Ettinger B**, Black DM, Nevitt MC, Rundle AC, Cauley JA, Cummings SR, Genant HK. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res* 1992; **7**: 449-456 [PMID: 1535172 DOI: 10.1002/jbmr.5650070413]
- 92 **Genant HK**, Jergas M, Palermo L, Nevitt M, Valentin RS, Black D, Cummings SR. Comparison of semiquantitative visual and quantitative morphometric assessment of prevalent and incident vertebral fractures in osteoporosis The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res* 1996; **11**: 984-996 [PMID: 8797120 DOI: 10.1002/jbmr.5650110716]
- 93 **Seeley DG**, Browner WS, Nevitt MC, Genant HK, Scott JC, Cummings SR. Which fractures are associated with low appendicular bone mass in elderly women? The Study of Osteoporotic Fractures Research Group. *Ann Intern Med* 1991; **115**: 837-842 [PMID: 1952469 DOI: 10.7326/0003-4819-115-11-837]
- 94 **Stone KL**, Seeley DG, Lui LY, Cauley JA, Ensrud K, Browner WS, Nevitt MC, Cummings SR. BMD at multiple sites and risk of fracture of multiple types: long-term results from the Study of Osteoporotic Fractures. *J Bone Miner Res* 2003; **18**: 1947-1954 [PMID: 14606506]
- 95 **Center JR**, Nguyen TV, Schneider D, Sambrook PN, Eisman JA. Mortality after all major types of osteoporotic fracture in men and

- women: an observational study. *Lancet* 1999; **353**: 878-882 [PMID: 10093980 DOI: 10.1016/S0140-6736(98)09075-8]
- 96 **Melton LJ**. Who has osteoporosis? A conflict between clinical and public health perspectives. *J Bone Miner Res* 2000; **15**: 2309-2314 [PMID: 11127196 DOI: 10.1359/jbmr.2000.15.12.2309]
- 97 **Ross PD**, Davis JW, Epstein RS, Wasnich RD. Pain and disability associated with new vertebral fractures and other spinal conditions. *J Clin Epidemiol* 1994; **47**: 231-239 [PMID: 8138833 DOI: 10.1016/0895-4356(94)90004-3]
- 98 **Borgström F**, Zethraeus N, Johnell O, Lidgren L, Ponzer S, Svensson O, Abdon P, Ornstein E, Lunsjö K, Thorngren KG, Sernbo I, Rehnberg C, Jönsson B. Costs and quality of life associated with osteoporosis-related fractures in Sweden. *Osteoporos Int* 2006; **17**: 637-650 [PMID: 16283064 DOI: 10.1007/s00198-005-0015-8]
- 99 **Peasgood T**, Herrmann K, Kanis JA, Brazier JE. An updated systematic review of Health State Utility Values for osteoporosis related conditions. *Osteoporos Int* 2009; **20**: 853-868 [PMID: 19271098 DOI: 10.1007/s00198-009-0844-y]

P- Reviewer: Cheung WH, Lee YK, Vulcano E
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Injuries in jumpers - are there any patterns?

Brett Rocos, Tim J Chesser

Brett Rocos, Tim J Chesser, Department of Trauma and Orthopaedics, Southmead Hospital, Bristol BS10 5NB, United Kingdom

Author contributions: Rocos B and Chesser TJ contributed equally to this work.

Conflict-of-interest statement: The authors declare no conflicts of interest regarding this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Brett Rocos, MRCS, Orthopaedic Trauma Fellow, Department of Trauma and Orthopaedics, Southmead Hospital, North Bristol NHS Trust, Bristol BS10 5NB, United Kingdom. brett.rocos@bristol.ac.uk
 Telephone: +44-117-9505050
 Fax: +44-117-9505050

Received: May 28, 2015
 Peer-review started: June 1, 2015
 First decision: July 10, 2015
 Revised: October 16, 2015
 Accepted: December 13, 2015
 Article in press: December 15, 2015
 Published online: March 18, 2016

Abstract

Suicide as a cause of death, affects every health system, and is a particular problem in heavily urbanised states and low and middle income countries (which account for 75% of suicide deaths). The World Health Organisation records that 800000 commit suicide each year, representing 1.4% of annual global deaths, and that suicide was the second leading cause of death in 15-29

year-olds across the world in 2012. In the United Kingdom, jumping from height accounts for 3%-5% of the 140000 suicide attempts annually is similar incidence to the rest of Europe. The Medline and EMBASE were interrogated for studies examining suicide caused by jumping from height. Manual screening of titles and abstracts was used to identify relevant works before data was extracted and systematically reviewed to identify the characteristics of a patient who jumps from height to commit suicide, delineate their patterns of injury and explore techniques that could be used to limit its occurrence. Emergency departments receiving patients who jump from a height need to have an understanding of the potential pathology that is likely to be encountered in order to deliver multidisciplinary, efficient and timely care in order that the impact of this devastating physical, psychological and social problem could be modified to the benefit of the patients involved.

Key words: Polytrauma; Suicide; Fracture

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This paper examines the incidence of injuries following a deliberate fall from height, and argues that there are predictable patterns of injury following this mechanism.

Rocos B, Chesser TJ. Injuries in jumpers - are there any patterns? *World J Orthop* 2016; 7(3): 182-187 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/182.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.182>

INTRODUCTION

Suicide, as a cause of death, affects every global health system, and is a particular problem in low and middle income countries (which account for 75% of suicide deaths) and in heavily urbanised states^[1-5]. More than

800000 commit suicide each year. The World Health Organisation records that 1.4% of annual global deaths are caused by suicide, and that suicide was the second leading cause of death in 15-29 year-olds across the world in 2012^[1,6-9].

Jumping from height accounts for 3%-15% of the 140000 suicide attempts in the United Kingdom each year, a similar incidence to the rest of Europe but lower than the 26% incidence found in California^[7,9-15]. Jumping requires no equipment and is easily carried out with little planning, and is likely to be fatal with 55% of patients dying either at the scene within an emergency department^[16-18].

Emergency departments that receive patients who jump from a height need to have an understanding of the potential pathology that is likely to be encountered in order to deliver organised and timely care to these patients. The management of these patients requires a multidisciplinary approach and involves the consumption of significant resource^[19]. When it is considered that patients are most often of working age in low to middle income countries, this becomes particularly relevant as the social and economic consequences as suboptimal management of a patient can be devastating to a family unit.

By identifying the characteristics of a patient who jumps from height for suicidal purposes, delineating their patterns of injury and exploring measures that could be used to limited the incidence of deliberate falls, the impact of this devastating physical, psychological and social problem could modified to the benefit of the patients involved.

RESEARCH METHODS

Using the OVID portal (Wolters Kluwer, Alphen aan den Rijn, the Netherlands), both Medline (1950-Present) and EMBASE (1980 to 2015 week 16) were searched for studies examining the subject. The search was conducted using the term suicide (mapped to MeSH headings) in combination with synonyms for jump (jump, leap, fall, autokabales). Abstracts identified were then screened manually for relevance and data extracted.

THE JUMPER AND THE JUMP

The jumper

Suicide is a desperate conclusion to a psychological problem, one that may have been diagnosed prior to the attempt or may have yet to be found. Several attempts have been made to describe the characteristics of a patient who attempts suicide by jumping from a high place. Gore-Jones *et al.*^[11] and others have described the jumping patient as a 31-year-old single person with a diagnosis of a psychotic illness or borderline personality disorder, of which 60% will have had contact with mental health services^[20]. Work from our own unit in the United Kingdom shows that in a series of 41 patients a Caucasian male aged 25-30 years is the most common

patient to present with this mechanism, a picture also seen in the United States^[20,21]. Other work has shown conflicting descriptors of patients. Chia and several European studies show that jumpers were usually female, young and single whereas many other reports show that jumping is more common in males^[7,9,13,17,20,22-25].

Other demographics of the patient group have been identified. Whilst eighty percent of patients show features that the act was impulsive, three in every four patients have made previous suicide attempts^[11]. Furthermore, Choi *et al.*^[16] showed that patients who jumped had a lower final grade of education, showing that severe injury following an attempt was associated with having attained a high school diploma rather than a university degree, perhaps indicating the social-economic situation in which the patient finds themselves at the time of their attempt.

Small *et al.*^[26] showed that inpatient suicide was a unique problem. The group showed that youth and social isolation in common with prolonged admission, a history of assaults and previous suicide attempts were particularly associated with jumping. Work in the inpatient population in the United Kingdom showed that jumping was likely to be the most common method of suicide for inpatients, as their access to alternative methods was likely to be restricted by virtue of sectioning or other controls in their environment^[14].

The presence of a psychotic illness in patients who jump is agreed on in all series' that examine the phenomenon. Psychosis may be diagnosed either before or after the attempt, but is typically made in association with the presentation. Estimates of pre-existing psychiatric illness, most commonly schizophrenia (which is more severe than that suffered by those who employ other methods of suicide) range from 10%-97%^[3,4,11,19,21,22,24,26-37]. Nielssen *et al.*^[29] examined a cohort of survivors of deliberate jumps from height and noted that only 44% of the cohort had a diagnosis of psychotic illness, of which 44% had received no previous treatment, suggesting that they were in their first episode of psychosis. Further exploration of the psychological state of these patients showed that 20% had a robust diagnosis of delusional psychosis, suggesting that the first episode of psychosis is a significant risk factor for suicide attempt^[29].

Although schizophrenia is the most often quoted psychotic diagnosis given to this cohort of patients, others diagnoses do feature. Stanford *et al.*^[35] found a diagnosis of personality disorder in 49%, depression in 25% and mood disorder in 18%. Kennedy *et al.*^[22] showed depression in 27% of patients, and Kontaxakis *et al.*^[24] showed affective psychosis-depressive type in several of their 46 patients. In contrast, our own cohort showed an absence of documented psychiatric disease either pre-existing or newly diagnosed during inpatient stay in 44% of patients; however depression features in 23% and psychosis in 13% of cases^[21]. Organic illness is found within the cohort more than one might expect given the young age of patients. Wong *et al.*^[4] showed that 44% of patients had physical illness, while others list

“serious somatic illness” as a comorbidity^[24]. Substance abuse also features in patient backgrounds with Bostman quoting 15% of Finnish patients suffering alcoholism at the time of their jump^[19,21,23,35].

The frequency of previous suicide attempt ranges from 23% to 75%^[11,22,38]. Alongside this, the methods of suicide do seem to change following a failed attempt. Paraschakis found that most patients who failed to commit suicide with self-poisoning, self-inflicted wrist laceration or jumping switched method to jumping on their subsequent attempts^[38]. Stanford reports a cohort of 55 patients with an 84% follow-up at a mean of 8 years, four had gone on to successful suicide^[35].

The jump

Unfortunately, 55% of deliberate falls cause death, a figure influenced by the height of the jump and the physical and psychological comorbidities^[16,17,39,40]. Dickinson *et al*^[17] examined a cohort of 117 patients attended by the London's Helicopter Air Ambulance Service who had fallen from height either accidentally or deliberately, and found that those who jumped rather than fell were more likely to die and that if head and chest injuries occurred, the height fall required for 50% of patients to die was found to be 11 m. If these injuries did not occur, the height fall required for 50% of patients to die increased to 22 m^[17]. Further study by Türk *et al*^[39] showed that suicidal falls occurred from a mean height of 23 m compared to 11 m for accidental falls, and that 79% of suicidal jumps were from a height greater than 16 m, whereas Copeland showed most suicidal falls were from 7 storeys (21 m) or higher^[23].

Deliberate jumps occur from a range of structures, including residential buildings in 63%-83% of cases, bridges and hotels^[4,14,25,32,36,40-44]. The prevention of suicide from bridges by the installation of barriers or other protections reduces the incidence of suicide from that site, an effect seen in both Europe and the United States^[8,9,14,25,36,42,43,45].

The surface that the patient lands on influences both injuries and survival. Whilst jumping from buildings is likely to end with a solid surface, jumping from a bridge could lead to landing on water. Gill^[46] showed that 77 suicides involving a jump into water showed few external signs of injury, suggesting drowning as the mode of death. Simonsen examined 10 cases of suicide with a water landing, and of the 10, drowning was the cause of death in six cases. Injuries, which were restricted to the thorax and spine, due to the fall caused death in four cases^[47].

THE INJURIES

The injury severity score correlates to the height of the jump and position of the patient on landing. It is established that those patients who survive their jump have multiple, severe injuries that usually require extensive treatment and that jumpers usually sustain injuries

to more than one body region^[18,28,48,49]. Each region of the body has particular injuries associated with it following a jump, each of which may give a clue as to the attitude of the patient on landing and help to guide both investigation and treatment.

The spine

The spine is the most commonly injured body region following a deliberate fall from height, an association that is magnified if sacral fractures are included into this category^[11,21,35,37,50-53]. Each group who have examined these injuries has identified a different spinal level as being most vulnerable. It seems that the most mobile spinal segments are particularly at risk particularly the thoracolumbar junction^[28,35]. Wirbel *et al*^[50] showed that of 36 patients with spinal injuries due to jumping, 33 had spinal injuries and Hahn *et al*^[51] showed that 83% of jumpers had fractures of the thoracolumbar spine, usually at the thoracolumbar junction. Li *et al*^[20] showed an incidence of 19% of neck injuries in their series, and Stanford *et al*^[35] showed in his series of 55 patients with spinal cord injury as a result of jumping, 23 patients (42%) had a complete cord injury with C5 and L1 being the most commonly injured levels. Our own series shows that 15/41 patients sustained a thoracolumbar fracture (37%) and 5/41 patients a cervical spine injury^[21].

The head

It is reasonable to hypothesise that primary brain injury is responsible for a significant proportion of the 55% of early deaths due to suicide *via* jumping, supported by Richter *et al*^[28] who showed that half of patients with a head injury fell or jumped from a single storey died^[16]. Abel *et al*^[41] showed that 30% of patients seen at their unit sustained craniofacial injuries, a figure in approximate agreement with Richter *et al*^[28] (27%) and our own series (29%)^[21]. However, Li *et al*^[20] showing an incidence of head injury of 70% in their series of 124 lethal falls or jumps, suggesting the conclusion that the head injury is often fatal. Head injury is further explored by Dickinson *et al*^[17] who showed that at a jump height of 11 m, 50% of those patients sustaining a head or chest injury die. Slightly contradictory to this, Türk *et al*^[39] showed that patients jumping from heights between 11-25 m, head injuries were less common than when patients jumped from heights outside this range, and that 79% of suicides were from 16 m or higher.

The pelvis

The only reports of pelvic fractures caused by a deliberate jump have been made by Roy-Camille *et al*^[53]. They describe an H-shaped transverse sacral fracture with vertical elements through the foramina. H-shaped fractures are now synonymous with the “Jumpers Fracture” are rare, with only 1.2% of pelvic fractures treated in a European trauma centre within a 9-year period being of this type^[52]. They are however significant injuries, requiring surgery in all displaced fractures, especially

with vertical shear fractures and associated L5 and S1 neurological damage^[52,53].

Teh *et al*^[48] found that their series of 57 jumpers showed a higher rate of pelvic injury in those who jumped from height when compared to fallers, and Richter *et al*^[28] found a 30% incidence of pelvic fracture amongst 39 jumpers with the incidence of pelvic injury increased significantly once the height of the jump was above 7 m^[48,51]. Within the cohort in our unit, pelvic fractures were found in 14/41 patients (34%), with jumpers fractures sustained in 4 of these, perhaps refuting a causal link between jumping and jumpers fractures^[21,53]. Pelvic injuries due to jumping come with poorer long-term results when compared to other causes of pelvic fracture. It is evident that these patients have a lower health related quality of life score than other pelvic fracture patients, and that patients who are younger at the time of injury fare better when compared to more elderly^[54].

The limbs

The limbs are intuitively the most vulnerable to injury with any significant trauma and in jumping^[50]. However, the degree to which they are injured and the pattern in which those injuries are found is not well described. Jumpers appear to sustain significantly more bilateral limb injuries than fallers which tend to be metaphyseal and epiphyseal^[28,48,49]. Hahn *et al*^[51] reported a limb fracture incidence to be 45% with calcaneal and ankle fracture to be the most common extremity injuries seen, with a respective incidence of 65% and 27%. Li *et al*^[20] showed a 28% incidence of extremity fracture in jumpers, and Katz *et al*^[37] showed that the lower limbs were the most common skeletal injury. These figures fall short of our own, where we found a 93% incidence of lower limb injury in our series of jump survivors^[21]. No studies have yet published regarding the relative incidences of open and closed fractures in jumpers, although one would expect a tendency toward a higher incidence of open fractures in this group, due to the higher energy. Only two studies reporting on upper limb injuries. Our own work has shown an incidence of 8/41 upper limb injuries (most often open fractures), and Hahn *et al*^[51] identified a 25% incidence of upper limb fracture in 39 jumpers^[21].

The thorax and abdomen

Injuries to the thorax are associated with death in the jumper^[17]. Chest injuries occur in up to 66% of jumpers, with abdominal injuries occurring much less frequently, estimated at being present in 6% of cases^[20,28,41]. Dickinson details how the presence of a chest injury was associated with a higher risk of death, and that in the absence of chest (and head) injuries reduced the risk^[17].

Abdominal injuries are rarely reported with one study reporting an incidence of 48% of abdominal injuries in a series of 139 fatal falls and jumps^[20]. This figure varies from other published and raw data both of which

give figure of 6% or less^[21,28]. It may be that abdominal injuries, similar to cervical spine and head injuries, are often fatal in the very early stages (through massive haemorrhage or visceral trauma) and so could be over-represented in the fatalities.

PATTERNS OF INJURY

Few papers have commented on the patterns of injury sustained by jumpers. As is seen above, every region of the body is affected by the trauma, and the trauma can affect a patient of any background, gender or age, with their concomitant influences on presentation and survival. It is difficult to categorise the injuries sustained to a particular attitude of landing or height of jump.

Richter *et al*^[28] has stated that no significant differences exist in the pattern of traumatic injuries caused by either accidental falling or deliberate jumping. Dickinson *et al*^[17] showed that jumpers have a higher injury severity score and mortality than fallers and Abel *et al*^[41] showed that 56% of patients who jump from bridges died from polytrauma rather than drowning or accompanying substance ingestion.

CONCLUSION

By recognising the common injury patterns of suicide attempts from jumping, the treating clinician can target investigation and treatment to severe and easily missed injury, the Jumpers fracture being the most obvious example. Outcomes are difficult to report in this patient population, but they almost all require multidisciplinary management. Patients presenting after jumping from a height should undergo routine screening of their head, chest, abdomen, pelvis and spine, and it is of course mandatory to address the psychological issues which lead to the suicide attempt.

REFERENCES

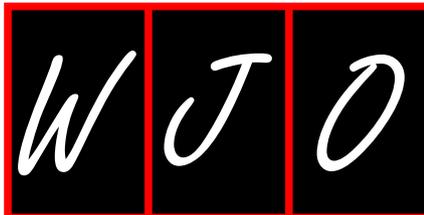
- 1 **World Health Organisation.** Preventing suicide: A global imperative. Geneva: World Health Organisation, 2014
- 2 **Ajdacic-Gross V,** Weiss MG, Ring M, Hepp U, Bopp M, Gutzwiller F, Rössler W. Methods of suicide: international suicide patterns derived from the WHO mortality database. *Bull World Health Organ* 2008; **86**: 726-732 [PMID: 18797649 DOI: 10.2471/BLT.07.043489]
- 3 **Chia BH,** Chia A, Ng WY, Tai BC. Suicide methods in singapore (2000-2004): types and associations. *Suicide Life Threat Behav* 2011; **41**: 574-583 [PMID: 21916950 DOI: 10.1111/j.1943-278X.2011.00055.x]
- 4 **Wong PW,** Caine ED, Lee CK, Beautrais A, Yip PS. Suicides by jumping from a height in Hong Kong: a review of coroner court files. *Soc Psychiatry Psychiatr Epidemiol* 2014; **49**: 211-219 [PMID: 23881109 DOI: 10.1007/s00127-013-0743-6]
- 5 **Pajonk FG,** Gruenberg KA, Moecke H, Naber D. Suicides and suicide attempts in emergency medicine. *Crisis* 2002; **23**: 68-73 [PMID: 12500891 DOI: 10.1027//0227-5910.23.2.68]
- 6 **World Health Organization.** The global burden of disease-estimates for 2000-2012. [accessed 2015 Jul 29]. Available from: URL: http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html

- 7 **Värnik A**, Kõlves K, Allik J, Arensman E, Aromaa E, van Audenhove C, Bouleau JH, van der Feltz-Cornelis CM, Giupponi G, Gusmão R, Kopp M, Marusic A, Maxwell M, Oskarsson H, Palmer A, Pull C, Realo A, Reisch T, Schmidtke A, Pérez Sola V, Wittenburg L, Hegerl U. Gender issues in suicide rates, trends and methods among youths aged 15-24 in 15 European countries. *J Affect Disord* 2009; **113**: 216-226 [PMID: 18625519 DOI: 10.1016/j.jad.2008.06.004]
- 8 **Hepp U**, Stulz N, Unger-Köppel J, Ajdacic-Gross V. Methods of suicide used by children and adolescents. *Eur Child Adolesc Psychiatry* 2012; **21**: 67-73 [PMID: 22130898 DOI: 10.1007/s00787-011-0232-y]
- 9 **Varnik A**, Kolves K, van der Feltz-Cornelis CM, Marusic A, Oskarsson H, Palmer A, Reisch T, Scheerder G, Arensman E, Aromaa E, Giupponi G, Gusmão R, Maxwell M, Pull C, Szekely A, Sola VP, Hegerl U. Suicide methods in Europe: a gender-specific analysis of countries participating in the "European Alliance Against Depression". *J Epidemiol Community Health* 2008; **62**: 545-551 [PMID: 2569832 DOI: 10.1136/jech.2007.065391]
- 10 Trends in Suicide-Health Statistics Quarterly. [accessed 2015 Jul 29]. Available from: URL: <http://www.ons.gov.uk/ons/rel/hsq/health-statistics-quarterly/no--20--winter-2003/index.html>
- 11 **Gore-Jones V**, O'Callaghan J. Suicide attempts by jumping from a height: a consultation liaison experience. *Australas Psychiatry* 2012; **20**: 309-312 [PMID: 22767939 DOI: 10.1177/1039856212449672]
- 12 Suicide - Causes - NHS Choices. Department of Health. [accessed 2015 Jul 29]. Available from: URL: <http://www.nhs.uk/Conditions/suicide/Pages/Causes.aspx>
- 13 **de Pourtalès MA**, Hazen C, Cottencin O, Consoli SM. [Adolescence, substance abuse and suicide attempt by jumping from a window]. *Presse Med* 2010; **39**: 177-186 [PMID: 19944561 DOI: 10.1016/j.lpm.2009.03.012]
- 14 **Gunnell D**, Nowers M. Suicide by jumping. *Acta Psychiatr Scand* 1997; **96**: 1-6 [PMID: 9259217 DOI: 10.1111/j.1600-0447.1997.tb09897.x]
- 15 **Hadjizacharia P**, Brown CV, Teixeira PG, Chan LS, Yang K, Salim A, Inaba K, Rhee P, Demetriades D. Traumatic suicide attempts at a level I trauma center. *J Emerg Med* 2010; **39**: 411-418 [PMID: 18996669 DOI: 10.1016/j.jemermed.2008.04.031]
- 16 **Choi JH**, Kim SH, Kim SP, Jung KY, Ryu JY, Choi SC, Park IC. Characteristics of intentional fall injuries in the ED. *Am J Emerg Med* 2014; **32**: 529-534 [PMID: 24612594 DOI: 10.1016/j.ajem.2014.01.053]
- 17 **Dickinson A**, Roberts M, Kumar A, Weaver A, Lockey DJ. Falls from height: injury and mortality. *J R Army Med Corps* 2012; **158**: 123-127 [PMID: 22860503 DOI: 10.1136/jramc-158-02-11]
- 18 **Beale JP**, Wyatt JP, Beard D, Busuttill A, Graham CA. A five year study of high falls in Edinburgh. *Injury* 2000; **31**: 503-508 [PMID: 10908743 DOI: 10.1016/S0020-1383(00)00034-6]
- 19 **Böstman OM**. Suicidal attempts by jumping from heights. A three-year prospective study of patients admitted to an urban university accident department. *Scand J Soc Med* 1987; **15**: 119-203 [PMID: 3497439]
- 20 **Li L**, Smialek JE. The investigation of fatal falls and jumps from heights in Maryland (1987-1992). *Am J Forensic Med Pathol* 1994; **15**: 295-299 [PMID: 7879771]
- 21 **Rocos B**, Acharya M, Chesser TJ. The Pattern of Injury and Workload Associated with Managing Patients After Suicide Attempt by Jumping from a Height. *Open Orthop J* 2015; **9**: 395-398 [PMID: 26401162 DOI: 10.2174/1874325001509010395]
- 22 **Kennedy P**, Rogers B, Speer S, Frankel H. Spinal cord injuries and attempted suicide: a retrospective review. *Spinal Cord* 1999; **37**: 847-852 [PMID: 10602527 DOI: 10.1038/sj.sc.3100932]
- 23 **Copeland AR**. Suicide by jumping from buildings. *Am J Forensic Med Pathol* 1989; **10**: 295-298 [PMID: 2589289 DOI: 10.1097/0000433-198912000-00004]
- 24 **Kontaxakis V**, Markidis M, Vaslamatzis G, Ioannidis H, Stefanis C. Attempted suicide by jumping: clinical and social features. *Acta Psychiatr Scand* 1988; **77**: 435-437 [PMID: 3389178 DOI: 10.1111/j.1600-0447.1988.tb05146.x]
- 25 **Bennewith O**, Nowers M, Gunnell D. Effect of barriers on the Clifton suspension bridge, England, on local patterns of suicide: implications for prevention. *Br J Psychiatry* 2007; **190**: 266-267 [PMID: 17329749 DOI: 10.1192/bjp.bp.106.027136]
- 26 **Small GW**, Rosenbaum JF. Nine psychiatric inpatients who leaped from a height. *Can J Psychiatry* 1984; **29**: 129-131 [PMID: 6722703]
- 27 **de Moore GM**, Robertson AR. Suicide attempts by firearms and by leaping from heights: a comparative study of survivors. *Am J Psychiatry* 1999; **156**: 1425-1431 [PMID: 10484956]
- 28 **Richter D**, Hahn MP, Ostermann PA, Ekkernkamp A, Muhr G. Vertical deceleration injuries: a comparative study of the injury patterns of 101 patients after accidental and intentional high falls. *Injury* 1996; **27**: 655-659 [PMID: 9039364 DOI: 10.1016/S0020-1383(96)00083-6]
- 29 **Nielssen O**, Glozier N, Babidge N, Reutens S, Andrews D, Gerard A, Malhi GS, Large MM. Suicide attempts by jumping and psychotic illness. *Aust N Z J Psychiatry* 2010; **44**: 568-573 [PMID: 20482416 DOI: 10.3109/00048671003606086]
- 30 **Sims A**, O'Brien K. Autokabalesis: an account of mentally ill people who jump from buildings. *Med Sci Law* 1979; **19**: 195-198 [PMID: 459744]
- 31 **Cantor CH**, Hill MA, McLachlan EK. Suicide and related behaviour from river bridges. A clinical perspective. *Br J Psychiatry* 1989; **155**: 829-835 [PMID: 2620210 DOI: 10.1192/bjp.155.6.829]
- 32 **Anderson J**, Allan DB. Vertebral fracture secondary to suicide attempt: demographics and patient outcome in a Scottish spinal rehabilitation unit. *J Spinal Cord Med* 2011; **34**: 380-387 [PMID: 21903011 DOI: 10.1179/2045772311Y.0000000013]
- 33 **Huisman A**, van Houwelingen CA, Kerkhof AJ. Psychopathology and suicide method in mental health care. *J Affect Disord* 2010; **121**: 94-99 [PMID: 19539376 DOI: 10.1016/j.jad.2009.05.024]
- 34 **Reisch T**, Schuster U, Michel K. Suicide by jumping from bridges and other heights: social and diagnostic factors. *Psychiatry Res* 2008; **161**: 97-104 [PMID: 18799221 DOI: 10.1016/j.psychres.2007.06.028]
- 35 **Stanford RE**, Soden R, Bartrop R, Mikk M, Taylor TK. Spinal cord and related injuries after attempted suicide: psychiatric diagnosis and long-term follow-up. *Spinal Cord* 2007; **45**: 437-443 [PMID: 17339888 DOI: 10.1038/sj.sc.3102043]
- 36 **Nowers M**, Gunnell D. Suicide from the Clifton Suspension Bridge in England. *J Epidemiol Community Health* 1996; **50**: 30-32 [PMID: 8762350 DOI: 10.1136/jech.50.1.30]
- 37 **Katz K**, Gonen N, Goldberg I, Mizrahi J, Radwan M, Yosipovitch Z. Injuries in attempted suicide by jumping from a height. *Injury* 1988; **19**: 371-374 [PMID: 3267637 DOI: 10.1016/0020-1383(88)90124-6]
- 38 **Paraschakis A**, Michopoulos I, Douzenis A, Christodoulou C, Lykouras L, Koutsaftis F. Switching suicide methods in order to achieve lethality: a study of Greek suicide victims. *Death Stud* 2014; **38**: 438-442 [PMID: 24758213 DOI: 10.1080/07481187.2013.780111]
- 39 **Türk EE**, Tsokos M. Pathologic features of fatal falls from height. *Am J Forensic Med Pathol* 2004; **25**: 194-199 [PMID: 15322459]
- 40 **Hanzlick R**, Masterson K, Walker B. Suicide by jumping from high-rise hotels. Fulton County, Georgia, 1967-1986. *Am J Forensic Med Pathol* 1990; **11**: 294-297 [PMID: 2275464]
- 41 **Abel SM**, Ramsey S. Patterns of skeletal trauma in suicidal bridge jumpers: a retrospective study from the southeastern United States. *Forensic Sci Int* 2013; **231**: 399.e1-399.e5 [PMID: 23806345 DOI: 10.1016/j.forsciint.2013.05.034]
- 42 **Lester D**. Suicide by jumping from bridges. *Percept Mot Skills* 2005; **100**: 628 [PMID: 16060421 DOI: 10.2466/PMS.100.3.628-628]
- 43 **Rosen DH**. Suicide survivors. A follow-up study of persons who survived jumping from the Golden Gate and San Francisco-Oakland Bay Bridges. *West J Med* 1975; **122**: 289-294 [PMID: 1171558]
- 44 **Reisch T**, Schuster U, Michel K. Suicide by jumping and accessibility of bridges: results from a national survey in Switzerland.

- Suicide Life Threat Behav* 2007; **37**: 681-687 [PMID: 18275374 DOI: 10.1521/suli.2007.37.6.681]
- 45 **Kim H**, Colantonio A. Intentional traumatic brain injury in Ontario, Canada. *J Trauma* 2008; **65**: 1287-1292 [PMID: 19077615 DOI: 10.1097/TA.0b013e31817196f5]
- 46 **Gill JR**. Fatal descent from height in New York City. *J Forensic Sci* 2001; **46**: 1132-1137 [PMID: 11569555]
- 47 **Simonsen J**. Injuries sustained from high-velocity impact with water after jumps from high bridges. A preliminary report of 10 cases. *Am J Forensic Med Pathol* 1983; **4**: 139-142 [PMID: 6858999]
- 48 **Teh J**, Firth M, Sharma A, Wilson A, Reznik R, Chan O. Jumpers and fallers: a comparison of the distribution of skeletal injury. *Clin Radiol* 2003; **58**: 482-486 [PMID: 12788319 DOI: 10.1016/S0009-9260(03)00064-3]
- 49 **Petaros A**, Slaus M, Coklo M, Sosa I, Cengija M, Bosnar A. Retrospective analysis of free-fall fractures with regard to height and cause of fall. *Forensic Sci Int* 2013; **226**: 290-295 [PMID: 23422164 DOI: 10.1016/j.forsciint.2013.01.044]
- 50 **Wirbel RJ**, Olinger A, Karst M, Mutschler WE. Treatment of severe injuries caused by attempted suicide: pattern of injury and influence of the psychiatric disorder on the postoperative course. *Eur J Surg* 1998; **164**: 109-113 [PMID: 9537717 DOI: 10.1080/110241598750004751]
- 51 **Hahn MP**, Richter D, Ostermann PA, Muhr G. [Injury pattern after fall from great height. An analysis of 101 cases]. *Unfallchirurg* 1995; **98**: 609-613 [PMID: 8584940]
- 52 **Zeman J**, Pavelka T, Matějka J. [Suicidal jumper's fracture]. *Acta Chir Orthop Traumatol Cech* 2010; **77**: 501-506 [PMID: 21223831]
- 53 **Roy-Camille R**, Saillant G, Gagna G, Mazel C. Transverse fracture of the upper sacrum. Suicidal jumper's fracture. *Spine (Phila Pa 1976)* 1985; **10**: 838-845 [PMID: 4089659]
- 54 **Borg T**, Holstad M, Larsson S. Quality of life in patients operated for pelvic fractures caused by suicide attempt by jumping. *Scand J Surg* 2010; **99**: 180-186 [PMID: 21044937 DOI: 10.1177/145749691009900314]

P- Reviewer: Daniels AH, Godoy-Santos AL
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D





Retrospective Study

Outcomes of tenodesis of the long head of the biceps tendon more than three months after rupture

Patrick J McMahon, Andrea Speziali

Patrick J McMahon, McMahon Orthopedics and Rehabilitation, University of Pittsburgh, Pittsburgh, PA 15203, United States

Patrick J McMahon, Andrea Speziali, Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA 15203, United States

Andrea Speziali, Institute of Orthopaedics and Traumatology, Catholic University, Agostino Gemelli's Hospital, 00168 Rome, Italy

Author contributions: McMahon PJ and Speziali A contributed to conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, making critical revisions related to important intellectual content of the manuscript, and final approval of the version of the article to be published; McMahon PJ and Speziali A contributed equally to this work.

Informed consent statement: All study participants, or their legal guardian, provide informed written consent prior to study enrollment.

Conflict-of-interest statement: No funding or financial support had been received by the authors. No potential sources of conflict of interest to disclose.

Data sharing statement: Participants gave informed consent for data sharing.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Patrick J McMahon, MD, Adjunct Associate Professor, Department of Bioengineering, University of Pittsburgh, 2100 Jane St, Pittsburgh, PA 15203, United States. mcmahonp@upmc.edu

Telephone: +1-412-4317342

Fax: +1-412-4317341

Received: February 3, 2015

Peer-review started: February 4, 2015

First decision: July 6, 2015

Revised: December 3, 2015

Accepted: December 18, 2015

Article in press: December 20, 2015

Published online: March 18, 2016

Abstract

AIM: To demonstrate that long head of the biceps tendon (LHBT) tenodesis is possible more than 3 mo after rupture.

METHODS: From September 2009 to January 2012 we performed tenodesis of the LHBT in 11 individuals (average age 56.9 years, range 42 to 73) more than 3 mo after rupture. All patients were evaluated by Disabilities of the Arm Shoulder and Hand (DASH) and Mayo outcome scores at an average follow-up of 19.1 mo. We similarly evaluated 5 patients (average age 58.2 years, range 45 to 64) over the same time treated within 3 mo of rupture with an average follow-up of 22.5 mo.

RESULTS: Tenodesis with an interference screw was possible in all patients more than 3 mo after rupture and 90% had good to excellent outcomes but two had recurrent rupture. All of those who had tenodesis less than 3 mo after rupture had good to excellent outcomes and none had recurrent rupture. No statistical difference was found for DASH and Mayo outcome scores between the two groups ($P < 0.05$).

CONCLUSION: Tenodesis of LHBT more than 3 mo following rupture had outcomes similar to tenodesis done within 3 mo of rupture but recurrent rupture

occurred in 20%.

Key words: Popeye deformity; Chronic rupture; Biceps tenodesis; Muscular spasm; Interference screw; Long head of biceps tendon

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: While some think long head of the biceps tendon (LHBT) tenodesis is not possible more than 3 mo after rupture, we have demonstrated that it is and will yield to outcomes similar to tenodesis done within 3 mo. The LHBT tenodesis was achieved in all patients affected by chronic rupture.

McMahon PJ, Speziali A. Outcomes of tenodesis of the long head of the biceps tendon more than three months after rupture. *World J Orthop* 2016; 7(3): 188-194 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/188.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.188>

INTRODUCTION

Rupture of the long head of the biceps tendon (LHBT) is common, accounting for 96% of all biceps brachii injuries^[1] and is generally treated non-operatively. The LHBT is a flexor of the elbow and a supinator of the forearm and also it flexes and medially rotates the shoulder^[2].

Studies that focused on results following chronic LHBT rupture^[3-5] have found disabilities could include persistent muscle pain, biceps spasm, strength loss and popeye deformity. The loss of strength has been reported at the elbow, not the shoulder, and is not insignificant. Soto-Hall and Stroot^[6] reported a 20% loss of elbow flexion strength, Deutch *et al.*^[3] demonstrated a 23% loss of supination strength and a 28% loss of flexion strength at the elbow and Sturzenegger *et al.*^[5] found a strength deficiency of 16% in flexion and 12% in supination. The popeye deformity is a cosmetic abnormality resulting from distal displacement of the long head of the biceps muscle that in part, gives the appearance of the biceps muscle being bigger.

Despite the popeye deformity and loss of elbow strength, few patients have persistent pain and muscle spasm after LHBT rupture so most are satisfied with non-operative treatments. In the past, surgery has been almost exclusively reserved for active patients with acute rupture within 3 mo of rupture and persistent symptoms^[7-9].

Acute tenodesis of LHBT rupture has yielded good to excellent results in most patients. Mariani *et al.*^[10] performed a tenodesis to the proximal humeral shaft within 12 wk of rupture and, after 13 years, only 7.4% of patients reported mild to moderate bicipital pain, 37% reported mild to moderate deformity at the biceps, 14.8% subjective weakness at the elbow and

only 11.1% poor clinical outcome and arm disability. Gumina *et al.*^[11] performed a tenodesis of the LHBT to the coracoid process less than 10 d after rupture and good to excellent clinical outcomes in 78.6% of patients. Tangari *et al.*^[12] performed a tenodesis into the bicipital groove after an average of 3 d following rupture. By 5 mo, none reported abnormal cosmetic appearance of the biceps and all of them returned to their professional activity.

But some patients first seek treatment more than 3 mo after rupture and in some the diagnosis is missed. Also, it is often difficult to predict those that will have persistent symptoms with non-operative treatment and lastly, tenolysis of the LHBT can result in pain and biceps spasm that persist more than 3 mo after rupture.

Tenodesis more than 3 mo after LHBT rupture has been thought to be complicated by scarring and retraction of the biceps tendon that precludes success^[13,14]. So, most surgeons do not offer surgery for individuals more than 3 mo after rupture. A case report of LHBT tenodesis 18 mo after rupture found return to full activity and no popeye deformity 6 mo later^[15]. In a prior series of 11 symptomatic patients who were treated at least 3 mo after rupture while the LHBT was too short for the authors' preferred method of tenodesis in 6, 3 reported normal cosmetic appearance and patient subjective self-assessments of strength and pain were satisfactory in over 70%^[14].

The purpose of this study is to report the surgical technique and objective clinical outcomes in a series of patients with LHBT tenodesis done more than 3 mo after rupture. First, we hypothesize that LHBT tenodesis done more than 3 mo after LHBT rupture can be done reliably with an interference screw technique. Second, we hypothesize that the outcomes will be similar to those within 3 mo of rupture.

MATERIALS AND METHODS

From September 2009 to January 2012 tenodesis of LHBT rupture was performed in 16 patients by a single surgeon (PJM). Exclusion criteria were: (1) previous surgery on the affected shoulder; (2) osteoarthritis of the glenohumeral joint; and (3) age > 75 years. All patients complained of biceps pain, weakness and persistent spasm of the biceps muscle with resisted elbow flexion activities (Tables 1 and 2) and were informed and gave their consent to the procedure and participation in the study. While there was a "popeye" deformity of the biceps muscle following a traumatic event, such as heavy lifting, or a fall, or while playing hockey, none had surgery for cosmetic reasons alone. The patients were divided into two groups, chronic which was more than 3 mo after rupture and acute which was less than or equal to 3 mo. In the chronic group 11 patients, one female and ten males, underwent LHBT tenodesis more than 3 mo after rupture and the mean time from rupture to surgery was 30.1 (range: 3.5 to 240) mo (Table 3). Two patients reported they had LHBT rupture and associated disabilities for 20 years and "several years", respectively.

Table 1 Pre-operative associated disabilities: Chronic group

Patient	Pain	Muscular spasm	Popeye deformity ¹
1	Moderate ³	+ ²	+
2	Moderate ³	+ ²	+
3	Moderate ³	+ ²	+
4	Severe ³	+ ²	+
5	Moderate ²	+ ²	+
6	Moderate ³	+ ²	+
7	Moderate ³	+ ³	+
8	Moderate ³	+ ²	+
9	Severe ³	+ ³	+
10	Moderate ³ /severe ²	+ ²	+
11	Moderate ³	+ ²	+

¹Popeye biceps sign; ²Intermittent during specific activities; ³Persistent.

All the patients in this group had failed to improve after a rehabilitation program. In the acute group were included 5 patients, all males, who underwent tenodesis 1.7 (1 to 2) mo after LHBT rupture (Table 4). All patients had a shoulder arthroscopy prior to the open biceps surgery.

The mean age at the time of the surgery was 56.9 (42 to 73) years in the chronic group and 58.2 (45 to 64) years in the acute group. Occupation was varied and included manual laborers, managers and retired individuals. In the chronic group, ten patients were right-handed and seven ruptured the right side. In the acute group, all patients were right-handed and three ruptured the right side.

Each patient had a deltopectoral incision about 6 cm in length and the superior 1 cm of the pectoralis tendon insertion onto the humerus is incised and the posterior pectoralis tendon was probed with a finger. This was where the proximal LHBT had often retracted and scarred and if it could be palpated, it is then hooked with the finger and brought into the wound and freed from the pectoralis tendon using sharp dissection. More often, the LHBT was difficult to palpate at the posterior pectoralis tendon and then a separate 4 cm incision was made at the superior aspect of the popeye muscle. After dissection through the subcutaneous tissue the myotendinous junction of the long head of the biceps muscle was palpated and the LHBT was palpated and freed with fingers in both incisions, most often from its scarred location posterior to the pectoralis. It was then brought out of the distal wound (Figure 1A) and the end of the tendon was resected with a scalpel. This separate incision at the superior aspect of the popeye muscle was used as prior attempts to find the LHBT with a deltopectoral incision alone often resulted in the LHBT being difficult to find or too short for interference screw fixation. In pilot study, indentifying the tendon distally and then using both incisions to dissect the scarred tendon from the posterior pectoralis tendon resulted in a robust and long tendon. Tenodesis was done with more tension in those greater than 3 mo after rupture than in those less than 3 mo; we tensioned the tenodesis with the elbow flexed 60 degrees (Figure 1B). We performed a suprapectoralis tenodesis with fixation at the bottom

Table 2 Pre-operative associated disabilities: Acute group

Patients	Pain	Muscular spasm	Popeye deformity ¹
1	Moderate ³	+ ²	+
2	Moderate ³	+ ²	+
3	Moderate ³	+ ²	+
4	Moderate ³	+ ²	+
5	Moderate ³	+ ²	+

¹Popeye biceps sign; ²Intermittent during specific activities; ³Persistent.

of the bicipital groove by re-routing the tendon from the distal incision to the proximal incision under the pectoralis tendon. Fixation in all patients was with a bioabsorbable interference screw (Figure 2, DePuy, Mitek, Inc, MA, USA). The normal appearance of the biceps muscle was restored.

After the procedure, the patient’s arm is placed in a sling. A few days after surgery, the patient began pendulum exercises and elbow stiffness resolved within 2 wk of surgery. Active ROM was begun at 4 wk and strengthening was begun at 3 mo after the surgery.

The self-assessment of symptoms and function of the upper extremity were evaluated with the Disabilities of the Arm Shoulder and Hand (DASH) questionnaire which evaluates the disabilities of the arm, shoulder and hand with a score from 0 (no symptoms, full function) to 100 (most severe disability)^[16]. For assessment of elbow function, the Mayo elbow performance score was administered which includes 45 points for pain, 20 for motion, 10 for stability and 25 for daily activities^[17]. An overall score more than 90 means excellent, from 89 to 75 is good, from 75 to 60 is fair and less than 60 is poor.

Statistical analysis

Statistical analysis was performed with the Mann-Whitney test to compare the DASH and Mayo scores between the two groups and with the Wilcoxon signed-rank test to compare the pre- and post-operative scores within the same group, significance was set at *P* < 0.05 (IBM-SPSS statistics). Lastly, a power analysis was performed with G*Power 3.1.5 version ($\alpha = 0.05, \beta = 0.80$).

RESULTS

No infection, stiffness or other complications were found following LHBT tenodesis in any of the patients. At an average follow-up of 19.1 (range: 9 to 35) mo, 10 patients were available in the chronic group: 9 (90%) patients reported full recovery to daily work and sports activities, no biceps pain, no spasm and the strength was comparable with the opposite side (Table 5).

Two patients had a popeye deformity of the biceps (20%) but only one of them (10%) had a poor outcome with recurrent muscular spasm, mild to moderate persistent pain and weakness at the biceps.

At an average follow-up of 22.5 (12 to 31.5) mo, 5 patients were available in the acute group: All the

Table 3 Patient demographics: Chronic group

Patient	Age (yr), sex, injured side	Rupture-to-surgery (mo)	Mechanism of rupture	Occupation
1	59, M, R ¹	4	Lifting	Minister
2	73, M, L ¹	6	Fall	Retired
3	68, M, L ¹	Several years	Unknown	Retired
4	56, F, L ¹	4	Lifting	Mental therapist
5	48, M, R ¹	6	Fall	Police officer
6	58, M, R ¹	8	Playing hockey	Teacher
7	42, M, R ¹	3.5	Lifting	Electrician
8	51, M, R ¹	240	Water skiing	Massage therapist
9	61, M, R ¹	12	Lifting	Retired
10	57, M, L ¹	13	Heavy lifting	Manager
11	53, M, R ²	5	Lifting	Carpenter

¹Right hand dominant; ²Ambidextrous. M: Male; F: Female; L: Left; R: Right.

Table 4 Patient demographics: Acute group

Patient	Age (yr), sex, injured side	Rupture-to-surgery (mo)	Mechanism of rupture	Occupation
1	60, M, R ¹	2	Heavy lifting	Retired
2	62, M, L ¹	2	Fall	Auto repair
3	60, M, R ¹	2	Heavy lifting	Technologist
4	64, M, R ¹	1.5	Lifting	Retired
5	45, M, L ¹	1	Lifting	Welder

¹Right hand dominant. M: Male; L: Left; R: Right.

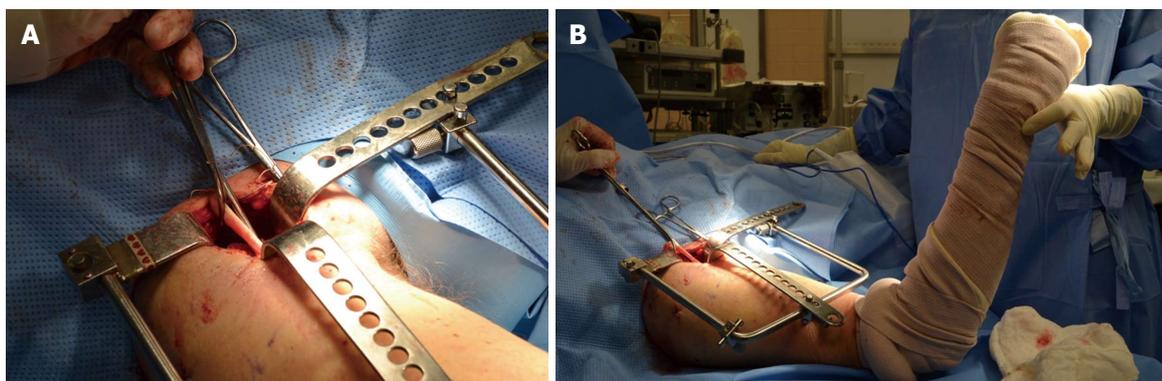


Figure 1 Intraoperative image. A: After incision of the proximal 1 cm insertion of the pectoralis tendon, the retracted and scarred long head of the biceps tendon is brought into the wound; B: Long head of the biceps tendon tenodesis is performed at 60° of elbow flexion.

patients reported full recovery to daily work and sports activities, no biceps pain, no spasm, strength was comparable to the opposite side (Table 6) and there were no popeye deformities.

In the chronic group the average pre-operative DASH score was 37.2 (range 29.2 to 55, $P = 0.859$) and at follow-up there was a significant improvement to 11.2 (range 0 to 35, $P = 0.679$) with a score change of 26 (range 20 to 29.2, $P = 0.001$). In the acute group the average pre-operative DASH score was 35.9 (range 30 to 45.8, $P = 0.859$) and the post-operative score was 7.3 (range 2.5 to 10.83, $P = 0.679$) showing a significant decrease of 28.6 (range 25.4 to 38.3, $P = 0.001$) points. We found no statistical significant difference between the two groups with the DASH score ($P = 0.679$).

In the chronic group the pre-operative Mayo perfor-

mance was 57.5 (range 45 to 70, $P = 1.0$) and at follow-up the average score significantly increased ($P = 0.001$) to 86 (range 85 to 100, $P = 0.859$). In the acute group the pre-operative Mayo performance score was poor in most the patients (mean score 57, range 50 to 65, $P = 1.0$), and there was a significant improvement ($P = 0.001$) to excellent or good in all the patients following surgery (mean score 91, range 85 to 100, $P = 0.859$). Statistical analysis showed no significant difference between the chronic and acute group in assessment with the Mayo performance score ($P = 0.859$).

DISCUSSION

LHBT tenodesis is possible more than 3 mo after rupture, and outcomes were similar to that after acute tenodesis.

Table 5 Physical exam of the shoulder: Pre- and post-operative strength in the chronic group

Patient	Strength								
	Pre-op			Post-op			Contralateral		
	AB	ER	IR	AB	ER	IR	AB	ER	IR
1	4/5	4/5	3/5	4/5	4/5	4/5	5/5	5/5	5/5
2	2/5	3/5	3/5	2/5	3/5	3/5	3/5	5/5	5/5
3	4/5	5/5	4/5	4/5	5/5	5/5	4/5	5/5	5/5
4	4/5	4/5	3/5	4/5	4/5	4/5	5/5	5/5	5/5
5	3/5	4/5	3/5	3/5	4/5	4/5	5/5	5/5	5/5
6	5/5	5/5	3/5	5/5	4/5	4/5	5/5	5/5	5/5
7	5/5	5/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5
8	5/5	5/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5
9	4/5	4/5	4/5	4/5	5/5	5/5	5/5	5/5	5/5
10	5/5	5/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5
11	4/5	4/5	3/5	4/5	4/5	4/5	4/5	4/5	4/5

AB: Abduction; ER: External rotation at 0 degree of arm abduction; IR: Internal rotation at 0 degree of arm abduction.

Table 6 Physical exam of the shoulder: Pre- and post-operative strength in the acute group

Patient	Strength								
	Pre-op			Post-op			Contralateral		
	AB	ER	IR	AB	ER	IR	AB	ER	IR
1	4/5	4/5	3/5	4/5	4/5	4/5	5/5	5/5	5/5
2	4/5	4/5	4/5	4/5	5/5	5/5	5/5	5/5	5/5
3	4/5	4/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5
4	5/5	5/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5
5	4/5	5/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5

AB: Abduction; ER: External rotation at 0 degree of arm abduction; IR: Internal rotation at 0 degree of arm abduction.



Figure 2 Intraoperative image of the biceps tenodesis: Suprapectoralis tenodesis at the bottom of bicipital groove using 7 mm × 23 mm bioabsorbable interference screw (Milagro, DePuy Mitek, MA, United States).

In the chronic group, we found a 90% excellent to good clinical outcomes and a 20% rate of popeye deformity. Only 1 of the 2 patients with popeye deformity reported a poor outcome. This is comparable to results reported prior following acute LHBT tenodesis^[14]. Mariani *et al.*^[10] reported a mild to moderate biceps deformity in 37% of patients and a complete recovery of daily activities in 89% of patients. De Carli *et al.*^[18] reported excellent to good clinical outcome in 94.2% of patients. Checchia *et al.*^[19] reported a 93.4% rate of satisfactory results. Hsu *et al.*^[20] reported a 25% incidence of recurrent rupture; Boileau *et al.*^[7] reported a 3% incidence of recurrent

rupture, 9% incidence of muscular cramping, and 30% rate of pain at the bicipital groove. Koh *et al.*^[21] reported 83.7% of excellent to good clinical outcomes, 4.6% incidence of cramping pain, and a 9.3% rate of recurrent rupture. Lastly, in a systematic review Slenker *et al.*^[22] found excellent to good clinical outcomes in 74% of patients, an 8% incidence of recurrent rupture, and a 24% rate of bicipital pain.

While chronic rupture of the LHBT is usually asymptomatic, successful biceps tenodesis is important for some active patients who suffer with long-term cramping, pain and weakness. It also is helpful in the treatment of patients with persistent symptoms who first seek treatment more than 3 mo after LHBT rupture and in others in whom the diagnosis was missed. It also eases the difficulty surgeons have in making the decision for surgery within 3 mo as contrary to the beliefs of most surgeons, if symptoms persist in the long-term, biceps tenodesis can still be successful. Lastly, when tenolysis of the LHBT results in pain and biceps spasm that persist for more than 3 mo, LHBT tenodesis is still possible.

Many proximal biceps tenodesis techniques, both arthroscopic^[13,23-26] and open^[12,27-29] have been described. We used interference screw fixation as prior biomechanical study had found it to have cyclic displacement and load at failure that are better than other fixation techniques immediately after surgery^[28]. No infection, stiffness or other complications were found consistent with prior studies that found low incidence

of complications after open LHBT tenodesis, specifically a 0.28% incidence of infection and a 0.28% incidence of neuropathies^[30]. After more than 3 mo from LHBT rupture, an arthroscopic tenodesis is not currently suitable for two reasons. First, the LHBT is usually retracted to the pectoralis tendon or distal to it. Second, the LHBT is sometimes short, warranting tenodesis more distal than usual.

There are few reports of tenodesis of chronic LHB ruptures. Tucker^[31] described their technique of chronic LHBT tenodesis in three patients but no results were reported. Ng and Funk^[14] reported their patient's subjective self-assessments of strength and pain and improvements of 74% and 79% respectively but only 3 of 11 patients had a normal cosmetic appearance. We achieved a normal cosmetic appearance in many more of our patients, 80% in all. This may have been partly from our retrieval of the LHBT with a separate 4 cm incision at the superior aspect of the "pop-eye" muscle when it could not be found with a deltopectoral incision, partly from our tensioning of the biceps tenodesis at 60° of elbow flexion and partly from our being able to reliably tenodesis the LHBT with an interference screw. Different from prior studies, we also performed objective scores and our improvements in these scores surpassed those prior demonstrated to be clinically relevant^[32,33].

Our study has several limitations. More patients with chronic rupture were included in the study because the senior author was known in his community that he was willing to operate on them. Still, the number of patients is small and while an interference screw could reliably be used for the tenodesis, surgeons should counsel patients and be prepared for other techniques in accordance with prior study^[14] despite the surgical improvements we report. In addition, associated morbidities could have influenced the outcome scores however the Popeye deformity was restored in 80%. While there were no statistical differences between the outcome scores after chronic and acute tenodesis, there were 2 recurrent ruptures in the chronic group and none in the acute group. A post hoc power analysis revealed that over a thousand of patients would be required to detect a statistical difference ($\alpha = 0.05$, $\beta = 0.8$) between outcome scores between the two groups.

COMMENTS

Background

The long head of the biceps tendon (LHBT) is a flexor of the elbow and a supinator of the forearm. Rupture of the LHBT is common, and is generally treated non-operatively. However disabilities could persist after LHBT rupture such as muscle pain, biceps spasm, strength loss and popeye deformity.

Research frontiers

Tenodesis more than 3 mo after LHBT rupture has been thought to be complicated by scarring and retraction of the biceps tendon that precludes success. So, most surgeons do not offer surgery for individuals more than 3 mo after rupture.

Innovations and breakthroughs

Contrary to what many surgeons think, tenodesis with an interference screw

more than 3 mo after LHBT rupture is possible and this confirmed the authors' hypothesis. Outcome is similar to that after tenodesis within 3 mo of rupture but there were 2 recurrent ruptures in those treated more than 3 mo after rupture. Those results are comparable to acute LHBT tenodesis recently performed by other authors (De Carli *et al.*, 2012; Koh *et al.*, 2010; Gumina *et al.*, 2011; Ng and Funk, 2012).

Applications

Tenodesis after LHBT rupture should be considered for patients with persistent complaints of pain, weakness and biceps muscle spasm and should not be limited to those within 3 mo of rupture. It also is helpful in the treatment of patients with persistent symptoms who first seek treatment more than 3 mo after LHBT rupture and in others in whom the diagnosis was missed. It also eases the difficulty surgeons have in making the decision for surgery within 3 mo as contrary to the beliefs of most surgeons, if symptoms persist in the long-term, biceps tenodesis can still be successful.

Terminology

Bicep tenodesis: This procedure involves the reattachment of the LHBT to the humeral bone. A guide wire and reamer is used to make a bone tunnel in the humerus; Interference screw: The fixation of the LHBT into the humeral bone tunnel is performed using a resorbable threaded screw; Muscular spasm: Is a sudden involuntary contraction of a muscle, or a group of muscles, accompanied by pain, but is usually harmless and ceases after few minutes.

Peer-review

The authors investigated the outcomes of tenodesis of the long head of the biceps tendon more than 3 mo after rupture compared with those performed within 3 mo, and found that the outcomes are similar after 3 mo rupture to those within 3 mo rupture.

REFERENCES

- 1 **Carter AN**, Erickson SM. Proximal biceps tendon rupture: primarily an injury of middle age. *Phys Sportsmed* 1999; **27**: 95-101 [PMID: 20086727 DOI: 10.3810/psm.1999.06.888]
- 2 **Glozman R**, Jobe F, Tibone J, Moynes D, Antonelli D, Perry J. Dynamic electromyographic analysis of the throwing shoulder with glenohumeral instability. *J Bone Joint Surg Am* 1988; **70**: 220-226 [PMID: 3343266]
- 3 **Deutch SR**, Gelineck J, Johannsen HV, Sneppen O. Permanent disabilities in the displaced muscle from rupture of the long head tendon of the biceps. *Scand J Med Sci Sports* 2005; **15**: 159-162 [PMID: 15885036 DOI: 10.1111/j.1600-0838.2004.00421.x]
- 4 **Klonz A**, Reilmann H. [Biceps tendon: diagnosis, therapy and results after proximal and distal rupture]. *Orthopade* 2000; **29**: 209-215 [PMID: 10798230]
- 5 **Sturzenegger M**, Béguin D, Grünig B, Jakob RP. Muscular strength after rupture of the long head of the biceps. *Arch Orthop Trauma Surg* 1986; **105**: 18-23 [PMID: 3707303 DOI: 10.1007/BF00625654]
- 6 **Soto-Hall R**, Stroot JH. Treatment of ruptures of the long head of the biceps brachii. *Am J Orthop* 1960; **2**: 192-193
- 7 **Boileau P**, Baqué F, Valerio L, Ahrens P, Chuinard C, Trojani C. Isolated arthroscopic biceps tenotomy or tenodesis improves symptoms in patients with massive irreparable rotator cuff tears. *J Bone Joint Surg Am* 2007; **89**: 747-757 [PMID: 17403796 DOI: 10.2106/JBJS.E.01097]
- 8 **Elser F**, Braun S, Dewing CB, Giphart JE, Millett PJ. Anatomy, function, injuries, and treatment of the long head of the biceps brachii tendon. *Arthroscopy* 2011; **27**: 581-592 [PMID: 21444012]
- 9 **Walch G**, Edwards TB, Boulahia A, Nové-Josserand L, Neyton L, Szabo I. Arthroscopic tenotomy of the long head of the biceps in the treatment of rotator cuff tears: clinical and radiographic results of 307 cases. *J Shoulder Elbow Surg* 2005; **14**: 238-246 [PMID: 15889020 DOI: 10.1016/j.jse.2004.07.008]
- 10 **Mariani EM**, Cofield RH, Askew LJ, Li GP, Chao EY. Rupture of the tendon of the long head of the biceps brachii. Surgical versus nonsurgical treatment. *Clin Orthop Relat Res* 1988; **(228)**: 233-239

- [PMID: 3342572]
- 11 **Gumina S**, Carbone S, Perugia D, Perugia L, Postacchini F. Rupture of the long head biceps tendon treated with tenodesis to the coracoid process. Results at more than 30 years. *Int Orthop* 2011; **35**: 713-716 [PMID: 20680275 DOI: 10.1007/s00264-010-1099-0]
 - 12 **Tangari M**, Carbone S, Gallo M, Campi A. Long head of the biceps tendon rupture in professional wrestlers: treatment with a mini-open tenodesis. *J Shoulder Elbow Surg* 2011; **20**: 409-413 [PMID: 20888263 DOI: 10.1016/j.jse.2010.08.008]
 - 13 **Richards DP**, Burkhart SS. Arthroscopic-assisted biceps tenodesis for ruptures of the long head of biceps brachii: The cobra procedure. *Arthroscopy* 2004; **20** Suppl 2: 201-207 [PMID: 15243459 DOI: 10.1016/j.arthro.2004.04.049]
 - 14 **Ng CY**, Funk L. Symptomatic chronic long head of biceps rupture: Surgical results. *Int J Shoulder Surg* 2012; **6**: 108-111 [PMID: 23493581 DOI: 10.4103/0973-6042.106222]
 - 15 **Cope MR**, Ali A, Bayliss NC. Biceps rupture in body builders: three case reports of rupture of the long head of the biceps at the tendon-labrum junction. *J Shoulder Elbow Surg* 2004; **13**: 580-582 [PMID: 15383821]
 - 16 **Angst F**, Schwyzer HK, Aeschlimann A, Simmen BR, Goldhahn J. Measures of adult shoulder function: Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) and its short version (QuickDASH), Shoulder Pain and Disability Index (SPADI), American Shoulder and Elbow Surgeons (ASES) Society standardized shoulder assessment form, Constant (Murley) Score (CS), Simple Shoulder Test (SST), Oxford Shoulder Score (OSS), Shoulder Disability Questionnaire (SDQ), and Western Ontario Shoulder Instability Index (WOSI). *Arthritis Care Res* (Hoboken) 2011; **63** Suppl 11: S174-S188 [PMID: 22588743 DOI: 10.1002/acr.20630]
 - 17 **Morrey BF**. Functional evaluation of the elbow. Morrey BF, editor. The elbow and its disorders. 3rd ed. Philadelphia: WB Saunders, 2000: 82
 - 18 **De Carli A**, Vadalà A, Zanzotto E, Zampar G, Vetrano M, Iorio R, Ferretti A. Reparable rotator cuff tears with concomitant long-head biceps lesions: tenotomy or tenotomy/tenodesis? *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 2553-2558 [PMID: 22349543]
 - 19 **Checchia SL**, Doneux PS, Miyazaki AN, Silva LA, Fregoneze M, Ossada A, Tsutida CY, Masiolo C. Biceps tenodesis associated with arthroscopic repair of rotator cuff tears. *J Shoulder Elbow Surg* 2005; **14**: 138-144 [PMID: 15789006]
 - 20 **Hsu AR**, Ghodadra NS, Provencher MT, Lewis PB, Bach BR. Biceps tenotomy versus tenodesis: a review of clinical outcomes and biomechanical results. *J Shoulder Elbow Surg* 2011; **20**: 326-332 [PMID: 21051241 DOI: 10.1016/j.jse.2010.08.019]
 - 21 **Koh KH**, Ahn JH, Kim SM, Yoo JC. Treatment of biceps tendon lesions in the setting of rotator cuff tears: prospective cohort study of tenotomy versus tenodesis. *Am J Sports Med* 2010; **38**: 1584-1590 [PMID: 20551285 DOI: 10.1177/0363546510364053]
 - 22 **Slenker NR**, Lawson K, Ciccotti MG, Dodson CC, Cohen SB. Biceps tenotomy versus tenodesis: clinical outcomes. *Arthroscopy* 2012; **28**: 576-582 [PMID: 22284407 DOI: 10.1016/j.arthro.2011.10.017]
 - 23 **Ahmad CS**, ElAttrache NS. Arthroscopic biceps tenodesis. *Orthop Clin North Am* 2003; **34**: 499-506 [PMID: 14984189 DOI: 10.1016/S0030-5898(03)00093-2]
 - 24 **Boileau P**, Krishnan SG, Coste JS, Walch G. Arthroscopic biceps tenodesis: a new technique using bioabsorbable interference screw fixation. *Arthroscopy* 2002; **18**: 1002-1012 [PMID: 12426544]
 - 25 **Gartsman GM**, Hammerman SM. Arthroscopic biceps tenodesis: operative technique. *Arthroscopy* 2000; **16**: 550-552 [PMID: 10882454]
 - 26 **Romeo AA**, Mazzocca AD, Tauro JC. Arthroscopic biceps tenodesis. *Arthroscopy* 2004; **20**: 206-213 [PMID: 14760357 DOI: 10.1016/j.arthro.2003.11.033]
 - 27 **Froimson AI**, O I. Keyhole tenodesis of biceps origin at the shoulder. *Clin Orthop Relat Res* 1975; (**112**): 245-249 [PMID: 1192640]
 - 28 **Mazzocca AD**, Rios CG, Romeo AA, Arciero RA. Subpectoral biceps tenodesis with interference screw fixation. *Arthroscopy* 2005; **21**: 896 [PMID: 16012508 DOI: 10.1016/j.arthro.2005.04.002]
 - 29 **Wiley WB**, Meyers JF, Weber SC, Pearson SE. Arthroscopic assisted mini-open biceps tenodesis: surgical technique. *Arthroscopy* 2004; **20**: 444-446 [PMID: 15067289]
 - 30 **Nho SJ**, Reiff SN, Verma NN, Slabaugh MA, Mazzocca AD, Romeo AA. Complications associated with subpectoral biceps tenodesis: low rates of incidence following surgery. *J Shoulder Elbow Surg* 2010; **19**: 764-768 [PMID: 20471866 DOI: 10.1016/j.jse.2010.01.024]
 - 31 **Tucker CJDA**. Tenodesis of isolated proximal ruptures of the long head of the biceps brachii. *Tech Shoulder Surg* 2009; **10**: 72-75 [DOI: 10.1097/BTE.0b013e3181a4474c]
 - 32 **Beaton DE**, Katz JN, Fossel AH, Wright JG, Tarasuk V, Bombardier C. Measuring the whole or the parts? Validity, reliability, and responsiveness of the Disabilities of the Arm, Shoulder and Hand outcome measure in different regions of the upper extremity. *J Hand Ther* 2001; **14**: 128-146 [PMID: 11382253 DOI: 10.1016/S0894-1130(01)80043-0]
 - 33 **Roy JS**, MacDermid JC, Woodhouse LJ. Measuring shoulder function: a systematic review of four questionnaires. *Arthritis Rheum* 2009; **61**: 623-632 [PMID: 19405008 DOI: 10.1002/art.24396]

P- Reviewer: Gao BL S- Editor: Song XX

L- Editor: A E- Editor: Li D



Retrospective Study

Knee awareness and functionality after simultaneous bilateral vs unilateral total knee arthroplasty

Roshan Latifi, Morten Grove Thomsen, Thomas Kallmose, Henrik Husted, Anders Troelsen

Roshan Latifi, Morten Grove Thomsen, Thomas Kallmose, Henrik Husted, Anders Troelsen, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, DK-2650 Hvidovre, Copenhagen, Denmark

Thomas Kallmose, Clinical Research Center, Copenhagen University Hospital Hvidovre, DK-2650 Hvidovre, Copenhagen, Denmark

Author contributions: Latifi R performed the initial drafting of manuscript; Latifi R and Thomsen MG collected the data; Latifi R, Thomsen MG, Kallmose T, Husted H and Troelsen A performed the data analysis, interpretation, the revision and final approval of manuscript; Thomsen MG, Husted H and Troelsen A designed the study.

Institutional review board statement: According to the national laws, questionnaire surveys and retrospective studies are exempt from obtaining approval from the National Research Ethics Committee (equivalent to IRB) (see Committee Acts at <http://www.dnvk.dk/>).

Informed consent statement: According to the national laws, it is not required to obtain informed written consent prior to conducting questionnaire surveys. Subjects were sufficiently anonymized and cannot be identified. Data were handled according to the acts of the Danish National Data Protection Agency. The Danish National Data Protection Agency approved this study (AHH-2014-010).

Conflict-of-interest statement: There are no conflicts of interest related to the present study.

Data sharing statement: The technical appendix, statistical code, and dataset associated with the present study are available from the corresponding author at roshan_latifi@yahoo.com. The data used in this study were sufficiently anonymized, and the Danish National Data Protection Agency approved this study (AHH-2014-010).

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license,

which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Roshan Latifi, MD, Orthopedic Surgery Registrar, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, Kettegaard Alle 30, DK-2650 Hvidovre, Copenhagen, Denmark. roshan_latifi@yahoo.com
Telephone: +45-52-404772
Fax: +45-38-623782

Received: December 11, 2015
Peer-review started: December 14, 2015
First decision: January 4, 2016
Revised: January 9, 2016
Accepted: January 27, 2016
Article in press: January 29, 2016
Published online: March 18, 2016

Abstract

AIM: To investigate knee awareness and functional outcomes in patients treated with simultaneous bilateral vs unilateral total knee arthroplasty (TKA).

METHODS: Through a database search, we identified 210 patients who had undergone unilateral TKA (UTKA) and 65 patients who had undergone simultaneous bilateral TKA (SBTKA) at our institution between 2010 and 2012. All TKAs were cemented and cruciate retaining. The mean follow-up period was 3.2 (2 to 4) years. All the patients had symptomatic and debilitating unilateral or bilateral osteoarthritis for which all conservative and non-surgical treatments were failed, thus preoperatively the patients had poor functionality. All patients were asked to complete Forgotten Joint Score (FJS) and Oxford Knee Score (OKS) questionnaires. The patients were matched according to age, gender, year of surgery, Kellgren-Lawrence score and pre- and

postoperative overall knee alignment. The FJS and OKS questionnaire results of the two groups were then compared.

RESULTS: A mixed-effects model was used to analyze differences between SBTKA and UTKA. OKS: The mean difference in the OKS between the patients who had undergone SBTKA and those who had undergone UTKA was 1.5, which was not statistically significant (CI = -0.9:4.0, *P*-value = 0.228). The mean OKS of the SBTKA patients was 37.6 (SD = 9.0), and the mean OKS of the UTKA patients was 36.1 (SD = 9.9). FJS: The mean difference in the FJS between the patients who had undergone SBTKA and those who had undergone UTKA was 2.3, which was not statistically significant (CI = -6.2:10.8, *P*-value = 0.593). The mean FJS of the SBTKA patients was 59.9 (SD = 27.5), and the mean FJS of the UTKA patients was 57.5 (SD = 28.8).

CONCLUSION: SBTKA and UTKA patients exhibited similar joint functionality and knee awareness. Our results support the use of SBTKA in selected patients suffering from clinically symptomatic bilateral osteoarthritis.

Key words: Unilateral total knee arthroplasty; Knee awareness; Patient-reported outcomes; Simultaneous bilateral total knee arthroplasty; Forgotten Joint Score

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We investigated the functional outcomes and knee awareness of patients who had undergone simultaneous bilateral compared with those who had undergone unilateral total knee arthroplasty (TKA). To accomplish this, we used the well-known Oxford Knee Score and the recently introduced Forgotten Joint Score (FJS). The FJS is based on a novel concept, or a patient's ability to forget about an artificial joint as a result of successful treatment; this result is considered as the ultimate goal of joint replacement surgery. No differences in final outcomes were observed between the groups. Therefore, individuals for whom bilateral TKA is indicated should be offered this option.

Latifi R, Thomsen MG, Kallelose T, Husted H, Troelsen A. Knee awareness and functionality after simultaneous bilateral vs unilateral total knee arthroplasty. *World J Orthop* 2016; 7(3): 195-201 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i3/195.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i3.195>

INTRODUCTION

The number of patients undergoing simultaneous bilateral total knee arthroplasty (SBTKA) has steadily increased. Currently, approximately 6% of all total knee arthroplasties (TKAs) performed in the United States are simultaneous bilateral procedures^[1].

The potential benefits of SBTKA compared with staged procedures include a decreased length of hospitalization, decreased time under anesthesia, decreased rehabilitation time, and decreased cost to the healthcare system^[2-5]. The disadvantages of SBTKA include an increased need for blood transfusions and increased physiological stress induced by simultaneous surgery^[1,6-9]. Although these benefits and disadvantages are accepted in the medical community, it remains a matter of debate whether functional outcomes, pain relief and patient satisfaction are equivalent between bilateral and staged procedures.

The need to rehabilitate two knees after SBTKA could be hypothesized to result in inferior functional outcomes for each knee compared with those achieved following rehabilitation of a single knee, as in unilateral TKA (UTKA)^[10]. Furthermore, the increased length of time required to perform SBTKA compared with UTKA could result in inferior technical performance toward the end of the procedure. This decreased performance could possibly be reflected in functional outcomes and knee awareness^[11]. Hence, functional outcomes and knee awareness following SBTKA could be inferior following UTKA according to the two aforementioned hypotheses. If functional outcomes and knee awareness are indeed inferior after SBTKA relative to UTKA, then the indications for performing SBTKA will be limited, and reconsideration of current SBTKA treatment strategies will be warranted.

The purpose of this study was to compare knee awareness and functional outcomes between patients who had undergone SBTKA and those who had undergone primary UTKA.

MATERIALS AND METHODS

This study was performed in accordance with the Declaration of Helsinki of the World Medical Association.

In the current retrospective, matched, case-control cohort study, we identified 69 patients who had undergone SBTKA with insertion of prostheses with the same TKA design in both knees at our institution between January 2010 and December 2012. During that period, the same TKA design was used in 240 UTKA procedures. Selected patients had symptomatic and debilitating unilateral or bilateral osteoarthritis for which conservative and non-surgical treatments were failed. Hence, preoperatively all the patients had poor functional performance. These UTKA patients were enrolled in the study as controls. The large size of the UTKA group ensured that as many patients as possible could be matched. Patients who had undergone knee surgery before primary TKA or who had undergone revision surgery with replacement of the prosthetic components after primary TKA were excluded. All TKA procedures had been performed using a medial para-patellar approach and were cemented and cruciate retaining (AGC, Biomet, Warsaw, Indiana). Additionally, all procedures included patellar resurfacing. The AGC prosthesis is a widely used TKA system that demonstrated good clinical results and longevity in earlier

studies^[12-14]. All patients had undergone surgery in a fast-track setting and had followed the same standardized postoperative rehabilitation program^[15]. Patients had been selected for SBTKA if they had bilateral disabling osteoarthritis and no cardiopulmonary comorbidity (ASA 1 to 2).

Gender, age at the time of surgery and year of surgery were documented for all patients. Preoperative radiographs were available for all knees and were analyzed for the degree of osteoarthritis using the Kellgren-Lawrence (KL) grading scale^[16,17]. Pre- and postoperative anteroposterior knee anatomical alignment was measured using short-film radiographs according to the method described by Petersen *et al.*^[18]. The same observer performed all radiographic assessments.

SBTKA patients and UTKA controls were invited to participate in this study in January 2014. Each patient received Forgotten Joint Score (FJS) and Oxford Knee Score (OKS) questionnaires. The patients in the UTKA group received one set of questionnaires, whereas those in the SBTKA group received two sets of questionnaires, with one clearly marked for each knee. The questionnaire responses left 65 SBTKA and 210 UTKA patients eligible for matching and further analysis.

Each knee in the SBTKA group was matched 1:1 to the knees in the UTKA group regarding gender, age at the time of surgery, year of surgery, KL grade and pre- and postoperative anatomical knee alignment (Table 1). This resulted in a study cohort of 94 knees in 47 patients in the SBTKA group and 94 knees in 94 patients in the UTKA group. The FJS and OKS were then calculated and compared between the matched groups. The follow-up period in this study was 2 to 4 years (mean 3.2 years). A flow chart describing the study's participants can be found in Figure 1.

For all participants, the OKS was calculated. The range of the OKS is 0 to 48, with 48 being the best possible score^[19].

The FJS^[20] is based on a 12-item questionnaire that evaluates a patient's ability to forget about his or her artificial joint in everyday life (awareness of the knee). The range for the FJS is 0 to 100, with 100 being the best possible score; the properties of the FJS questionnaire have been reported in earlier studies^[20-22].

The data used in the current study were sufficiently anonymized, and The Danish National Data Protection Agency approved the project (AHH-2014-010).

Statistical analysis

The statistical methods used in this study were reviewed by Thomas Kalleose, a biomedical statistician from Clinical Research Center, Copenhagen University Hospital Hvidovre, Kettegaard Alle 30, DK-2650 Hvidovre, Copenhagen, Denmark.

Matching was performed for all patients who completed both the FJS and the OKS questionnaires. The matching was prioritized by operation year, gender,

KL score, age at the time of surgery, postoperative anatomical knee alignment and preoperative anatomical knee alignment. The year of surgery was most highly prioritized because of the small amount of overlap between the UTKA and the SBTKA patients. Pooled squared differences corresponding to age at the time of surgery, postoperative anatomical knee alignment and preoperative anatomical knee alignment were used to determine the best matching; 100000 permutations were used, and the best was selected based on the smallest pooled squared difference.

Sample size estimation was based on the ability to detect an inter-group difference (power 90%, *P*-level 0.05, SD: 10) of 5 points or more (considered to be clinically relevant) in the OKS. This resulted in a need for 85 cases per group.

A mixed-effects model was used to assess the differences between UTKA and SBTKA patients in terms of both the FJS and the OKS. The score difference between the UTKA and the SBTKA patients within each matched knee pair was used as an outcome in the model. Because of the assumed within-patient variance in the SBTKA group, a random effect corresponding to the SBTKA patients' scores was added. Because of the matching, no other factors were added to the model. A *P*-value less than 0.05 was considered statistically significant. All matching and analyses were performed using R 3.02 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

OKS

The mean difference in the OKS between the SBTKA and the UTKA groups was 1.5, which was not statistically significant (CI = -0.9:4.0, *P*-value = 0.228). The mean OKS was 37.6 (SD = 9.0) in the SBTKA group, and it was 36.1 (SD = 9.9) in the UTKA group (Table 2).

FJS

The mean difference in the FJS between the SBTKA and the UTKA groups was 2.3, which was not statistically significant (CI = -6.2:10.8, *P*-value = 0.593). The mean FJS was 59.9 (SD = 27.5) in the SBTKA group, and it was 57.5 (SD = 28.8) in the UTKA group (Table 2).

DISCUSSION

Whether the advantages of SBTKA outweigh its potential disadvantages has been a topic of much debate. Numerous studies have investigated the risk of perioperative complications after SBTKA^[1,4-9,23-29] and the cost-effectiveness of the procedure^[2,30-33] in comparison with UTKA. However, the majority of these studies have not focused on long-term functional outcomes or knee awareness. In the current study, we investigated functional outcomes and knee awareness during daily-living activities using patient-reported outcome measures following SBTKA and UTKA.

Table 1 Post-matching distribution of demographic parameters

		Bilateral	Unilateral
Gender, No. of knees (%)	Male	34 (36%)	34 (36%)
	Female	60 (64%)	60 (64%)
Age at operation, mean (SD) range		66 yr (8.2)	65 yr (7.4)
		45, 81	46, 80
Osteoarthritis grade, No. of knees (%)	KL 1 + 2	27 (29%)	27 (29%)
	KL 3 + 4	67 (71%)	67 (71%)
Alignment, mean (SD) range	Preoperative	1.2 (5.3)	1.3 (5.9)
	Postoperative	-16.3, 16.2 ¹	-12.1, 21.8 ¹
		5.2 (3.0)	4.9 (3.4)
Operation year, No. of knees (%)	2010	24 (26%)	24 (26%)
	2011	62 (66%)	62 (66%)
	2012	8 (9%)	8 (9%)

¹Varus (-), Valgus (+). KL: Kellgren-Lawrence.

We hypothesized that the longer duration required to perform SBTKA could lead to inferior technical performance when operating on the second knee and that difficulties during postoperative rehabilitation of two knees after SBTKA could result in an overall inferior functional outcome and higher knee awareness compared with those for UTKA. We found that the SBTKA group did not significantly differ from the UTKA group with respect to functional outcomes or knee awareness at 2 to 4 years post-surgery. This result is consistent with the findings from a previous study^[34], in which 150 consecutive, but selected, SBTKA cases were compared with 271 UTKA cases in a standardized fast-track setting between 2003 and 2009. Husted *et al.*^[34] demonstrated that the outcome at three months and two years was similar or better in the SBTKA group with regard to satisfaction, the range of motion, pain, the use of a walking aid and the ability to work and perform activities of daily living. However, this previous study did not use a validated PROM, such as those used in the present study.

In a retrospective review of 697 TKAs in 511 consecutive patients (SBTKA: 186, UTKA: 325) with bilateral knee arthritis and a follow-up period of 2 to 8 years, using the Knee Society Score and its subscales as endpoints, Bagsby and Pierson^[35] demonstrated a statistically significant better postoperative functional outcome, including an increased total range of motion ($P = 0.001$), improved flexion ($P = 0.003$), and an increased function score ($P < 0.001$) associated with SBTKA. They presumed that this finding was related to the absence of contralateral arthritis, which would produce pain and restrict rehabilitation. This contradicts our hypothesis that simultaneous surgeries on two knees would make rehabilitation more difficult and potentially result in an inferior outcome compared with that associated with UTKA. However, their findings are ultimately consistent with our conclusions regarding the

Table 2 Results for the Oxford Knee Score and Forgotten Joint Score

		SBTKA	UTKA
PROM outcomes, mean (SD) range	OKS	37.6 (9.0)	36.1 (9.9)
		10, 48	9, 48
	FJS	59.9 (27.5)	57.5 (28.8)
		0, 100	0, 100

FJS: Forgotten Joint Score; OKS: Oxford Knee Score; SBTKA: Simultaneous bilateral TKA; UTKA: Unilateral TKA; TKA: Total knee arthroplasty; PROM: Patient-reported outcome measure.

performance of SBTKA.

In a study by Zeni and Snyder-Mackler^[36], 15 subjects who had undergone SBTKA were observed prospectively for a period of 2 years. Subjects in this group were matched with subjects who had undergone UTKA by age, sex and BMI, providing equal samples of 15 subjects in each group. These 2 groups were then compared with a group of 21 orthopedically healthy subjects, which served as the control group. Pre- and post-operative self-reported functional measures and objective clinical tests were then applied to the groups. At 2 years, the long-term outcomes of the bilateral group were similar to those of the matched sample of patients who had undergone UTKA and to those of the control subjects. These findings are again in accordance with the findings of the current study, which unanimously support the practice of SBTKA according to the long-term outcomes.

Seo *et al.*^[11] reviewed SBTKA outcomes in 420 patients at 1 year post-surgery. Similar to what was hypothesized in the current study, they hypothesized that the postoperative results produced by SBTKA would vary as a result of disparate surgical scenarios between knees. In support of their hypothesis, they found that the second TKA had a greater incidence of outliers in limb coronal alignment (16.2% vs 9.0%, $P = 0.003$), more blood loss (735 mL vs 656 mL, $P < 0.001$) and a slightly longer operation time (61 min vs 58 min, $P < 0.001$) compared with the first TKA. This supports our hypothesis that lengthier surgeries could lead to inferior technical performance near the end of a procedure, possibly resulting in inferior functional outcomes and higher knee awareness of the knee operated on last. However, at the 1-year follow-up, neither knee showed a difference in its range of motion after surgery ($P = 1.000$). The postoperative flexion angle improved equally, to 129° and 127°. Moreover, no significant differences in the postoperative Knee Society Function Score or the total Western Ontario and McMaster Universities Arthritis Index scores were observed between the sides ($P = 0.316$ and 1.000, respectively).

However, a significant difference in the postoperative Knee Society Knee Score was observed ($P < 0.001$). Concerns that SBTKA produces inferior functional outcomes in one or both knees thus appear to be unwarranted.

A review of previous SBTKA studies concluded that there are no sound counterarguments against

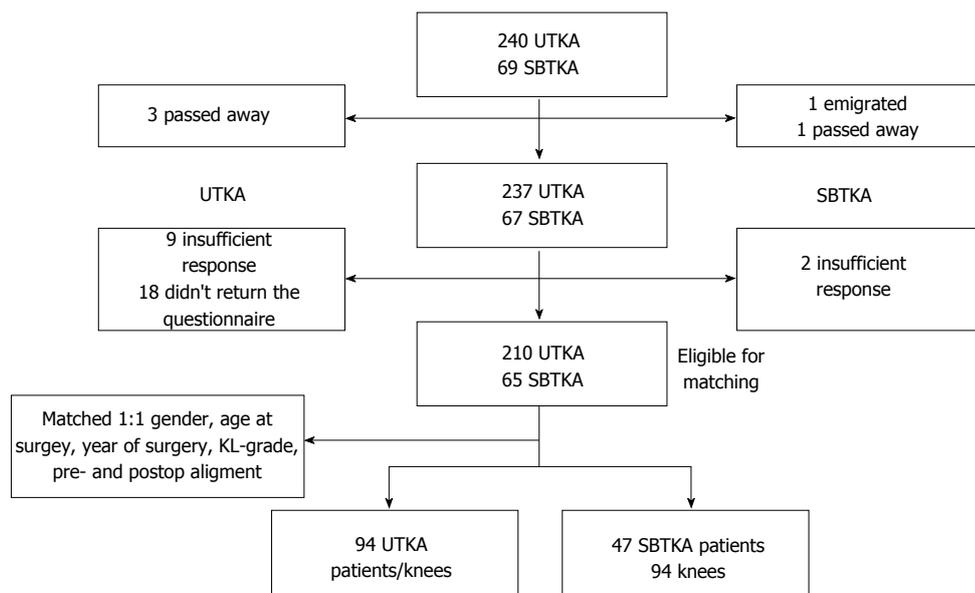


Figure 1 Flowchart describing the patients who were invited to participate in the study and those included in the analysis. UTKA: Unilateral TKA; SBTKA: Simultaneous bilateral TKA; TKA: Total knee arthroplasty; KL: Kellgren-Lawrence.

the orthopedic advantages of SBTKA^[8]. Any remaining debate centers on medical and anesthetic contraindications. Age and preoperative comorbidities play important roles in postoperative morbidity and mortality. In addition, 81% of the participants in the Consensus Conference on Bilateral Total Knee Arthroplasty Group^[37] agreed that SBTKA is associated with an increased risk of perioperative adverse events when performed on unselected patients. The consensus group also agreed that physicians and hospitals should consider using more restrictive patient selection criteria and should exclude those with a modified cardiac risk index greater than 3 to mitigate the potentially increased risk of adverse events. Furthermore, the entire group agreed that when there is a conflict between orthopedic need and medical adequacy with regard to SBTKA, the medical concern for a patient's safety should prevail over the orthopedic need. Hence, only patients with no evidence of cardiopulmonary disease, ASA scores of 1 or 2 and bilateral disabling osteoarthritis are considered as acceptable candidates for SBTKA at our institution. In the current study, because cardiopulmonary disease tends to increase with age, we found that patients in the SBTKA group were younger before matching was performed. It can be argued that younger patients might experience fewer degenerative changes in the knees. To account for this, we matched the SBTKA and UTKA groups in terms of gender, age at the time of surgery, year of surgery, KL grade and pre- and postoperative anatomical knee alignment to minimize potential bias.

The FJS has recently been introduced and validated as a post-surgical assessment tool for total joint replacement^[20]. The FJS specifically evaluates a patient's level of awareness of their artificial joint in 12 scenarios commonly encountered in daily life. Joint awareness includes strong sensations, such as pain, and the ability to

perform activities of daily living, as well as more subtle feelings, such as mild stiffness, subjective dysfunction and any other discomfort that a patient might encounter. The forgotten joint concept, which is based on the level of knee awareness, is a more discerning assessment method that has shown better discriminatory power and less of a ceiling effect than traditional questionnaires measuring pain or function do. These features are especially appealing for more active patients with good to excellent outcomes after TKA. The FJS also allows detection of potential subtle differences between patients and between follow-up time points^[20,21].

The current study has certain limitations. We matched patients according to the abovementioned parameters, whereas other factors (e.g., BMI, social status, psychological profile, preoperative duration and pain intensity, comorbidities and ASA score) that may potentially affect functional outcomes and knee awareness, were not accounted for in this study. However we have chosen parameters, which have a high influence on functional outcomes and involved in this study. The primary strength of the present study is the matching of patients between the study groups in terms of gender, age at the time of surgery, KL grade and pre- and postoperative knee alignment. Because of this matching procedure, we believe that our study groups are comparable, counteracting the study's limitations.

SBTKA and UTKA patients exhibit similar knee function and knee awareness. Our results support the use of SBTKA in selected patients without cardiopulmonary comorbidity who suffer from clinically symptomatic bilateral osteoarthritis.

COMMENTS

Background

The potential benefits of simultaneous bilateral total knee arthroplasty (TKA)

include a decreased overall length of hospitalization, shorter overall anesthesia time and decreased cost to both the patient and the institution. Although many prior studies examining differences between unilateral and bilateral TKA have focused on short-term postoperative outcomes, costs, and complications, few have assessed differences in long-term results and functional outcomes.

Research frontiers

To the authors' knowledge, this is the first review to analyze patient-reported outcomes (PROs) after simultaneous bilateral TKA using the newly introduced Forgotten Joint Score (FJS). The FJS was validated in Danish in a parallel study at the authors' institution and was used to compare PROs between simultaneous bilateral TKA patients and unilateral TKA patients.

Innovations and breakthroughs

Several reports have shown the potential effects of knee alignment on PRO measures after TKA. Therefore, the authors measured osteoarthritis severity and pre- and post-operative overall knee alignment based on the radiographs of 340 patients. Moreover, the authors used the forgotten joint concept, which is a more discerning assessment method that has shown better discriminatory power and less of a ceiling effect than traditional questionnaires measuring pain or function do. These features are especially appealing for more active patients with good to excellent outcomes after TKA. The authors obtained perfect matching regarding age, gender, year of surgery, Kellgren-Lawrence score and pre- and post-operative overall knee alignment, which allowed comparison of parameters of interest without confounding by other elements. Concurrently with the FJS, the authors also used the well-known Oxford Knee Score (OKS) to investigate patient functionality after joint replacement.

Applications

The results support the use of simultaneous bilateral TKA in selected patients without cardiopulmonary comorbidity who suffer from clinically symptomatic bilateral osteoarthritis.

Peer-review

This is an interesting retrospective study. The patients were evaluated using subjective scores (FJS and OKS Questionnaires) and therefore the results are "more reliable".

REFERENCES

- Memtsoudis SG, Mantilla CB, Parvizi J, Stundner O, Mazumdar M. Have bilateral total knee arthroplasties become safer? A population-based trend analysis. *Clin Orthop Relat Res* 2013; **471**: 17-25 [PMID: 23008025 DOI: 10.1007/s11999-012-2608-9]
- Kovacik MW, Singri P, Khanna S, Gradsar IA. Medical and financial aspects of same-day bilateral total knee arthroplasties. *Biomed Sci Instrum* 1997; **33**: 429-434 [PMID: 9731398]
- Dennis DA. Debate: bilateral simultaneous total knee arthroplasty. *Clin Orthop Relat Res* 2004; **428**: 82-83 [PMID: 15534523 DOI: 10.1097/01.blo.0000147133.75432.84]
- Patil N, Wakankar H. Morbidity and mortality of simultaneous bilateral total knee arthroplasty. *Orthopedics* 2008; **31**: 780-789; quiz 780-789 [PMID: 18714773 DOI: 10.3928/01477447-20080801-23]
- Stubbs G, Pryke SE, Tewari S, Rogers J, Crowe B, Bridgfoot L, Smith N. Safety and cost benefits of bilateral total knee replacement in an acute hospital. *ANZ J Surg* 2005; **75**: 739-746 [PMID: 16173984 DOI: 10.1111/j.1445-2197.2005.03516.x]
- Fabi DW, Mohan V, Goldstein WM, Dunn JH, Murphy BP. Unilateral vs bilateral total knee arthroplasty risk factors increasing morbidity. *J Arthroplasty* 2011; **26**: 668-673 [PMID: 20875943 DOI: 10.1016/j.arth.2010.07.011]
- Memtsoudis SG, Ma Y, González Della Valle A, Mazumdar M, Gaber-Baylis LK, MacKenzie CR, Sculco TP. Perioperative outcomes after unilateral and bilateral total knee arthroplasty. *Anesthesiology* 2009; **111**: 1206-1216 [PMID: 19934863 DOI: 10.1097/ALN.0b013e3181bfab7d]
- Noble J, Goodall JR, Noble DJ. Simultaneous bilateral knee replacement: a persistent controversy. *Knee* 2009; **16**: 420-426 [PMID: 19464899 DOI: 10.1016/j.knee.2009.04.009]
- Oakes DA, Hanssen AD. Bilateral total knee replacement using the same anesthetic is not justified by assessment of the risks. *Clin Orthop Relat Res* 2004; **428**: 87-91 [PMID: 15534525 DOI: 10.1097/01.blo.0000147133.75432.86]
- Bakirhan S, Angin S, Karatosun V, Ünver B, Günel I. Physical performance parameters during standing up in patients with unilateral and bilateral total knee arthroplasty. *Acta Orthop Traumatol Turc* 2012; **46**: 367-372 [PMID: 23268822 DOI: 10.3944/AOTT.2012.2684]
- Seo JG, Lee BH, Moon YW, Chang MJ, Park SH. Disparate postoperative results in the first and second knees on simultaneous bilateral total knee arthroplasty. *J Arthroplasty* 2014; **29**: 2331-2336 [PMID: 25131798 DOI: 10.1016/j.arth.2014.07.025]
- Ritter MA. The Anatomical Graduated Component total knee replacement: a long-term evaluation with 20-year survival analysis. *J Bone Joint Surg Br* 2009; **91**: 745-749 [PMID: 19483226 DOI: 10.1302/0301-620X.91B6.21854]
- Worland RL, Johnson GV, Alemparte J, Jessup DE, Keenan J, Norambuena N. Ten to fourteen year survival and functional analysis of the AGC total knee replacement system. *Knee* 2002; **9**: 133-137 [PMID: 11950577 DOI: 10.1016/S0968-0160(01)00146-6]
- Thomsen MG, Husted H, Otte KS, Holm G, Troelsen A. Do patients care about higher flexion in total knee arthroplasty? A randomized, controlled, double-blinded trial. *BMC Musculoskelet Disord* 2013; **14**: 127 [PMID: 23565578 DOI: 10.1186/1471-2474-14-127]
- Husted H, Holm G, Jacobsen S. Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. *Acta Orthop* 2008; **79**: 168-173 [PMID: 18484241 DOI: 10.1080/17453670710014941]
- Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis* 1957; **16**: 494-502 [PMID: 13498604 DOI: 10.1136/ard.16.4.494]
- Kijowski R, Blankenbaker D, Stanton P, Fine J, De Smet A. Arthroscopic validation of radiographic grading scales of osteoarthritis of the tibiofemoral joint. *AJR Am J Roentgenol* 2006; **187**: 794-799 [PMID: 16928947 DOI: 10.2214/AJR.05.1123]
- Petersen TL, Engh GA. Radiographic assessment of knee alignment after total knee arthroplasty. *J Arthroplasty* 1988; **3**: 67-72 [PMID: 3361322 DOI: 10.1016/S0883-5403(88)80054-8]
- Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br* 1998; **80**: 63-69 [PMID: 9460955 DOI: 10.1302/0301-620X.80B1.7859]
- Behrend H, Giesinger K, Giesinger JM, Kuster MS. The "forgotten joint" as the ultimate goal in joint arthroplasty: validation of a new patient-reported outcome measure. *J Arthroplasty* 2012; **27**: 430-436.e1 [PMID: 22000572 DOI: 10.1016/j.arth.2011.06.035]
- Thienpont E, Opsomer G, Koninckx A, Houssiau F. Joint awareness in different types of knee arthroplasty evaluated with the Forgotten Joint score. *J Arthroplasty* 2014; **29**: 48-51 [PMID: 23688851 DOI: 10.1016/j.arth.2013.04.024]
- Giesinger K, Hamilton DF, Jost B, Holzner B, Giesinger JM. Comparative responsiveness of outcome measures for total knee arthroplasty. *Osteoarthritis Cartilage* 2014; **22**: 184-189 [PMID: 24262431 DOI: 10.1016/j.joca.2013.11.001]
- Husted H. Fast-track hip and knee arthroplasty: clinical and organizational aspects. *Acta Orthop Suppl* 2012; **83**: 1-39 [PMID: 23205862 DOI: 10.3109/17453674.2012.700593]
- Andersen LØ, Husted H, Otte KS, Kristensen BB, Kehlet H. A compression bandage improves local infiltration analgesia in total knee arthroplasty. *Acta Orthop* 2008; **79**: 806-811 [PMID: 19085499 DOI: 10.1080/17453670810016894]
- Andersen LØ, Gaarn-Larsen L, Kristensen BB, Husted H, Otte KS, Kehlet H. Subacute pain and function after fast-track hip and knee arthroplasty. *Anaesthesia* 2009; **64**: 508-513 [PMID: 19413820 DOI: 10.1111/j.1365-2044.2008.05831.x]
- Bullock DP, Sporer SM, Shirreffs TG. Comparison of simultaneous

- bilateral with unilateral total knee arthroplasty in terms of perioperative complications. *J Bone Joint Surg Am* 2003; **85-A**: 1981-1986 [PMID: 14563808]
- 27 **Fick D**, Crane T, Shakespeare D. A comparison of bilateral vs. unilateral total knee arthroplasty mobilised using a flexion regime. *Knee* 2002; **9**: 285-289 [PMID: 12424036 DOI: 10.1016/S0968-0160(02)00038-8]
- 28 **Leonard L**, Williamson DM, Ivory JP, Jennison C. An evaluation of the safety and efficacy of simultaneous bilateral total knee arthroplasty. *J Arthroplasty* 2003; **18**: 972-978 [PMID: 14658100 DOI: 10.1016/S0883-5403(03)00282-1]
- 29 **Ritter MA**, Harty LD, Davis KE, Meding JB, Berend M. Simultaneous bilateral, staged bilateral, and unilateral total knee arthroplasty. A survival analysis. *J Bone Joint Surg Am* 2003; **85-A**: 1532-1537 [PMID: 12925634]
- 30 **Ritter MA**, Harty LD. Debate: simultaneous bilateral knee replacements: the outcomes justify its use. *Clin Orthop Relat Res* 2004; **428**: 84-86 [PMID: 15534524 DOI: 10.1097/01.blo.0000148784.17187.2f]
- 31 **Jankiewicz JJ**, Sculco TP, Ranawat CS, Behr C, Tarrentino S. One-stage versus 2-stage bilateral total knee arthroplasty. *Clin Orthop Relat Res* 1994; **309**: 94-101 [PMID: 7994981]
- 32 **Lane GJ**, Hozack WJ, Shah S, Rothman RH, Booth RE, Eng K, Smith P. Simultaneous bilateral versus unilateral total knee arthroplasty. Outcomes analysis. *Clin Orthop Relat Res* 1997; **345**: 106-112 [PMID: 9418627 DOI: 10.1097/00003086-199712000-00015]
- 33 **Reuben JD**, Meyers SJ, Cox DD, Elliott M, Watson M, Shim SD. Cost comparison between bilateral simultaneous, staged, and unilateral total joint arthroplasty. *J Arthroplasty* 1998; **13**: 172-179 [PMID: 9526210 DOI: 10.1016/S0883-5403(98)90095-X]
- 34 **Husted H**, Troelsen A, Otte KS, Kristensen BB, Holm G, Kehlet H. Fast-track surgery for bilateral total knee replacement. *J Bone Joint Surg Br* 2011; **93**: 351-356 [PMID: 21357957 DOI: 10.1302/0301-620X.93B3.25296]
- 35 **Bagsby D**, Pierson JL. Functional outcomes of simultaneous bilateral versus unilateral total knee arthroplasty. *Orthopedics* 2015; **38**: e43-e47 [PMID: 25611419 DOI: 10.3928/01477447-20150105-59]
- 36 **Zeni JA**, Snyder-Mackler L. Clinical outcomes after simultaneous bilateral total knee arthroplasty: comparison to unilateral total knee arthroplasty and healthy controls. *J Arthroplasty* 2010; **25**: 541-546 [PMID: 19356894 DOI: 10.1016/j.arth.2009.02.016]
- 37 **Mementsoudis SG**, Hargett M, Russell LA, Parvizi J, Cats-Baril WL, Stundner O, Sculco TP. Consensus statement from the consensus conference on bilateral total knee arthroplasty group. *Clin Orthop Relat Res* 2013; **471**: 2649-2657 [PMID: 23564364 DOI: 10.1007/s11999-013-2976-9]

P- Reviewer: Drosos GI, Willis-Owen CA

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 April 18; 7(4): 202-271



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

W**J****O****EDITORIAL**

- 202 Use of clinical movement screening tests to predict injury in sport
Chimera NJ, Warren M
- 218 Understanding the pathogenesis of hip fracture in the elderly, osteoporotic theory is not reflected in the outcome of prevention programmes
Guerado E, Sandalio RM, Caracuel Z, Caso E

REVIEW

- 229 Elbow ulnar collateral ligament injuries in athletes: Can we improve our outcomes?
Redler LH, Degen RM, McDonald LS, Altchek DW, Dines JS

MINIREVIEWS

- 244 Sternoclavicular joint dislocation and its management: A review of the literature
Morell DJ, Thyagarajan DS

ORIGINAL ARTICLE**Retrospective Cohort Study**

- 251 Promising short-term clinical results of the cementless Oxford phase III medial unicondylar knee prosthesis
van Dorp KB, Breugem SJM, Bruijn DJ, Driessen MJM
- 258 Ankle fracture configuration following treatment with and without arthroscopic-assisted reduction and fixation
Angthong C

Retrospective Study

- 265 Use of Ligament Advanced Reinforcement System tube in stabilization of proximal humeral endoprostheses
Stavropoulos NA, Sawan H, Dandachli F, Turcotte RE

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Sergio Hernandez-Sanchez, MSc, Physiotherapist, Professor, Physiotherapy Area, Pathology and Surgery Department, Faculty of Medicine, Miguel Hernandez University, 03550 Sant Joan D'alacant, Spain

AIM AND SCOPE

World Journal of Orthopedics (World J Orthop, WJO), online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Huan-Liang Wu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Xin Kong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLICATION DATE
 April 18, 2016

COPYRIGHT

© 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT

All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS

Full instructions are available online at http://www.wjnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION

<http://www.wjnet.com/esps/>

Use of clinical movement screening tests to predict injury in sport

Nicole J Chimera, Meghan Warren

Nicole J Chimera, Department of Athletic Training, Daemen College, Amherst, NY 14226, United States

Meghan Warren, Department of Physical Therapy and Athletic Training, Northern Arizona University, Flagstaff, AZ 86001, United States

Author contributions: Chimera NJ and Warren M contributed equally to writing and revising this manuscript.

Conflict-of-interest statement: Chimera NJ and Warren M have no conflicts of interest related to this publication.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Nicole J Chimera, PhD, ATC, CSCS, Department Chair and Program Director, Department of Athletic Training, Daemen College, 4380 Main Street, Amherst, NY 14226, United States. nchimera@daemen.edu
Telephone: +1-716-8398413
Fax: +1-716-8398314

Received: August 7, 2015
Peer-review started: August 11, 2015
First decision: October 16, 2015
Revised: October 28, 2015
Accepted: December 29, 2015
Article in press: January 4, 2016
Published online: April 18, 2016

Abstract

Clinical movement screening tests are gaining popularity as a means to determine injury risk and to implement training programs to prevent sport injury. While these

screens are being used readily in the clinical field, it is only recently that some of these have started to gain attention from a research perspective. This limits applicability and poses questions to the validity, and in some cases the reliability, of the clinical movement tests as they relate to injury prediction, intervention, and prevention. This editorial will review the following clinical movement screening tests: Functional Movement Screen™, Star Excursion Balance Test, Y Balance Test, Drop Jump Screening Test, Landing Error Scoring System, and the Tuck Jump Analysis in regards to test administration, reliability, validity, factors that affect test performance, intervention programs, and usefulness for injury prediction. It is important to review the aforementioned factors for each of these clinical screening tests as this may help clinicians interpret the current body of literature. While each of these screening tests were developed by clinicians based on what appears to be clinical practice, this paper brings to light that this is a need for collaboration between clinicians and researchers to ensure validity of clinically meaningful tests so that they are used appropriately in future clinical practice. Further, this editorial may help to identify where the research is lacking and, thus, drive future research questions in regards to applicability and appropriateness of clinical movement screening tools.

Key words: Functional Movement Screen; Y Balance Test; Star excursion balance test; Tuck jump analysis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Clinical movement screening tests like the Functional Movement Screen and Y Balance Test have gained a lot of popularity in the clinical setting as a tool to predict injury and guide injury prevention programs/training. However, clinicians should be aware that various factors like sex differences, previous injury history, and sport participation can influence the accuracy of these screening tests; therefore, it

is important to evaluate the validity, reliability, and accuracy of these tools before implementing them into clinical practice.

Chimera NJ, Warren M. Use of clinical movement screening tests to predict injury in sport. *World J Orthop* 2016; 7(4): 202-217 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/202.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.202>

INTRODUCTION

Injury is often unavoidable in sport participation and is reported to be as high as 2.51/1000 Athlete-Exposures^[1] and 13.79/1000 Athlete-Exposures^[2] in high school and collegiate athletes, respectively. These injuries are further classified as overuse, defined as an injury caused by repeated microtrauma without an identifiable event to attribute the mechanism of injury or acute, defined as a specific, identifiable mechanism of injury^[3]. Additionally, acute injuries occur as a result of either contact or non-contact mechanisms. Contact mechanisms as defined by the National Collegiate Athletic Association Injury Surveillance System^[4] involve direct contact with another player or the playing surface, apparatus/ball, or other in environment (*e.g.*, wall, fence); while non-contact mechanisms are identified as those that occur with no apparent contact and may involve a rotational force. Although these injury distinctions seem to be well understood, the effect of all potential mechanisms is less clear. Several clinical movement screening tests have been proposed to analyze differing mechanisms for injury prediction. Pre-season movement screening tests are likely less effective in predicting contact injuries due to the external mechanism involved with contact injuries. Thus, when comparing between studies one must be cognizant of the operational definition of injury.

Movement screening tools can be used for non-contact injury risk prediction and to guide injury prevention programs; however, the costly nature of sophisticated research equipment is a barrier to using high speed motion analysis in the practicing clinicians' pre-participation physical examinations. Therefore, clinician friendly movement screening tools have been developed and are gaining popularity as a means to reduce injury risk. These tools include the Functional Movement Screen™ (FMS), Y Balance/Star Excursion Balance Test (YBT/SEBT), Tuck Jump Assessment (TJA), Drop Jump Screening Test (DJST), and the Landing Error Scoring System (LESS), which are being used fairly regularly in the clinical setting. Thus, it is important to understand the research surrounding the applicability of these tools to non-contact injury prediction. Therefore, the purpose of this editorial is to define the above clinical movement screening tools and to address each test's normative data, validity, reliability, performance differences across samples,

Table 1 Fundamental movement patterns of the Functional Movement Screen™ and the associated clearing tests

Fundamental movement pattern	Clearing test
Deep squat	
Hurdle step ¹	
Inline lunge ¹	
Shoulder mobility ¹	Shoulder impingement test
Active straight leg raise ¹	
Trunk stability push-up	Spinal extension test
Rotatory stability ¹	Spinal flexion test

¹Performed and scored separately for the right and left side.

recommendations for use, and injury prediction.

FMS™

The FMS (Figure 1) is a clinical test developed to screen performance with fundamental movements, requiring a balance between stability and mobility while moving through a proximal to distal sequence^[5]. The FMS is a proprietary tool purported to measure fundamental movements necessary for athletic performance and comprises 7 individual movement patterns and 3 clearing tests, which are tests associated with some movement patterns to determine the presence of pain (Table 1)^[5,6]. Each movement pattern is scored based on degree of compensatory movements required to complete the movement, as well as pain. An ordinal scoring system is used from 3-0, where 3 corresponds to the ability to correctly complete the movement without compensation, 2 corresponds to performing the movement with compensation, 1 corresponds to the inability to perform the movement. A score of 0 is given if there is pain during any portion of the movement or pain with the corresponding clearing test. The sum of the 7 movement patterns is used to assess differences between groups and when testing bilaterally the lower score of the two limbs is used for total score calculation (max = 21). Asymmetry is noted in the 5 movements performed bilaterally: Hurdle step, inline lunge, shoulder mobility, active straight leg raise, and rotational stability. Asymmetry is calculated as the absolute difference between the right and left side with each of these movements.

The benefits of the FMS are that it is quick, inexpensive, and easy to administer. This screen is clinically relevant in that minimal equipment and training are required to administer and score the FMS, and a standard testing protocol is readily available^[5,6]. The FMS testing takes between 12-15 min to administer and score, making this a viable option for many. The FMS test kit (Functional Movement Systems, Inc., Chatham, VA) is approximately \$180.00, making it accessible for a wide variety of clinical and performance settings. Reliable and consistent scoring has been shown with just a 2 h training session^[7], again enhancing the use with a variety of fitness and healthcare professionals in different settings.

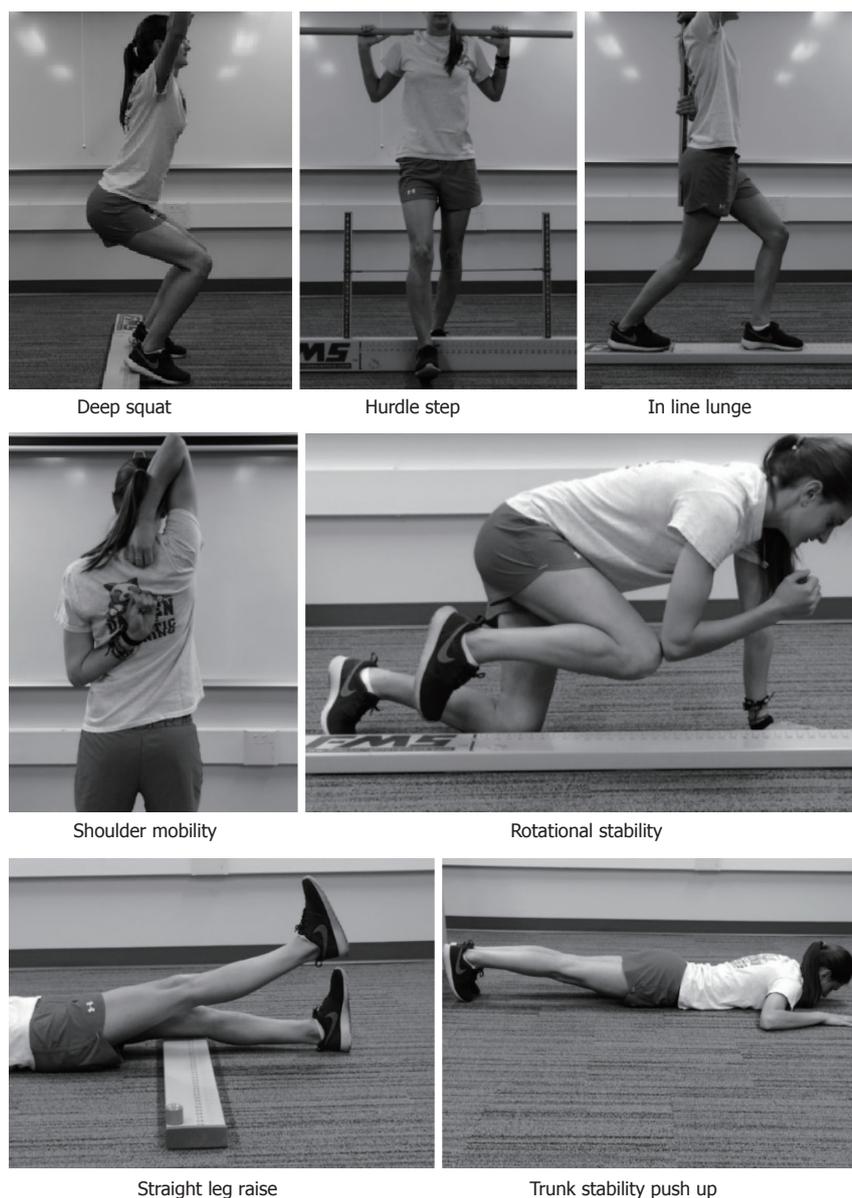


Figure 1 Images of the Functional Movement Screen.

Five studies utilizing varied samples have calculated normative values for the summed total FMS in the last 5 years^[8-12]. Two of the studies focused on small samples of participants in specific sports, hurling and Gaelic football ($n = 62$)^[8], and running ($n = 43$)^[9]. The normative value for the total FMS score in both of these studies was very similar (15.6 ± 1.5 for the hurlers and Gaelic football players and 15.4 ± 2.4 in the runners). Teyhen *et al.*^[11] reported a higher normative value for 247 male and female active service members at 16.2 ± 2.2 . There was a significant age by sex interaction ($P = 0.007$) with higher scores in females and younger ages. The largest sample ($n = 622$) of 21 years and older included males and females in the general population and reported age and sex stratified FMS scores^[10] in general FMS scores decreased with age and females had higher average FMS scores compared with men. Although a large study overall, care should be taken

with application of this population-based study since some of the age/sex categories were very small (for example: $n = 34$ for females 50-54 years old). Finally, normative data in a large ($n = 209$) sample of 18-40 years old physical active males and females reported an average FMS score of 15.7 ± 1.9 ^[10]. Taken together, for young to mid-life physically active males and females, normative FMS falls between 15.4 and 16.2 points. Lower FMS overall scores were reported for older ages^[12]. No differences in overall score between males and females were reported^[9,10,13], but sex differences were seen with specific movement patterns^[13].

The validity of the FMS has been assessed in several ways. First, for a screening test to be valid it must first be reliable. The reliability has been examined in several studies, and these studies have recently been summarized^[14]. Table 2 on Page 3574 gives an excellent summary of the FMS reliability studies^[14].

Table 2 Results of studies using Functional Movement Screen™ score of 14 as a cut point to predict musculoskeletal injuries

Ref.	Sample	Injury definition	Sensitivity	Specificity	+LR	-LR
Kiesel <i>et al</i> ^[22]	46 male professional American football players	Athletic performance injury requiring injury reserve and time loss of 3 wk	54%	91%	NR	NR
Chorba <i>et al</i> ^[23]	38 female Division II athletes	Athletic performance injury requiring intervention	58%	74%	2.20	NR
O'Connor <i>et al</i> ^[24]	874 male Officer candidates	Any injury: Physical training injury requiring intervention	45%	78%	NR	NR
		Overuse injury: Long term repetitive energy exchange with cumulative microtrauma	12%	90%	NR	NR
		Serious injury: Physical training injury requiring removal from training	12%	94%	NR	NR
Butler <i>et al</i> ^[25]	108 firefight trainees	Physical training injury with time loss of 3 consecutive days	84%	62%	2.20	0.26
Warren <i>et al</i> ^[26]	195 male and females Division I athletes	Athletic performance injury requiring intervention	54%	46%	NR	NR
Garrison <i>et al</i> ^[27]	160 male and females Division I athletes	Athletic performance injury requiring intervention, and 24 h missed time or splinting, to continue participation	67%	73%	2.51	0.45
Hotta <i>et al</i> ^[28]	84 competitive male runners	Physical training injury with time loss of 4 wk	73%	54%	NR	NR
Knapik <i>et al</i> ^[29]	1045 male and female military cadets	Physical training injury	55%	49%	NR	NR
McGill <i>et al</i> ^[30]	53 elite police officer	Back injury not due to specific acute incidents	28%	76%	NR	NR
		All injury	42%	47%	NR	NR

LR: Likelihood ratio.

Additionally, we previously studied inter- and intra-rater reliability of the FMS after a single 2 h training session^[7]. Four raters with different experience with FMS, and education scored 20 recreational athletes (10 males and 10 females) and then re-scored a week later. Two raters were experienced with FMS - one was a Physical Therapy (PT) student, and one was a cross country coach (also FMS certified). The 2 inexperienced FMS administrators were a faculty member in Athletic Training and a PT student. Inter-rater reliability was good for session 1 (ICC = 0.89; 95%CI: 0.80-0.95) and for session 2 (ICC = 0.87; 95%CI: 0.76-0.94). Intra-rater reliability was good for each rater, ranging from 0.81 to 0.91. The conclusions of this study are similar to others who assessed real-time, clinically applicable (*i.e.*, not video recorded) FMS reliability^[15-17].

The FMS has good face validity with movement experts (*i.e.*, physical therapists and athletic trainers) as the developers of the screen^[5,6]. The content validity is not known for much of the screen. One of the movement patterns - deep squat - has a published biomechanical analysis^[18]; it is currently not known what is occurring biomechanically with the other 6 movement patterns. Recently, the inline lunge was compared with measures of power, speed, and balance and no significant correlations were found^[19], pointing to the need for further research into what is occurring with each movement pattern.

The FMS has evolved into a single score as a straight summation the scores of the 7 fundamental movement pattern into a single score, ranging from 0-21. In this scoring algorithm, for those patterns performed bilaterally, the lower score of the right and left sides is used, and all patterns are equally weighted. Three of the movement patterns in the FMS (deep squat, hurdle

step, and inline lunge) are considered the "big three" with more complex movement patterns^[5,6]. The other 4 are considered the "little four" and it is recommended to intervene with these patterns first before addressing the more complex movements. Despite this, the single summative score weights all 7 patterns equally.

The construct validity of a single value has been assessed recently with two factor analyses of the FMS. Kazman *et al*^[20] administered the FMS to 934 Marine Officer candidates. With exploratory factor analysis, this study failed to show that FMS score was a unitary construct, calling into question the construct validity for a single score. No interpretable factor was found, and Cronbach's alpha showed low internal consistency; all of the movement patterns had scores below the pre-defined cut-point, suggesting a lack of clustering of the FMS movement patterns. The concept of unidimensionality was further explored in a study of 290 elite Chinese athletes^[21]; the results were consistent with Kazman *et al*^[20], demonstrating a lack of unitary construct; this suggests that the summed score does not reflect one latent measure or one single result. The authors cautioned about the use of a single summed score, and instead suggested focusing on each movement pattern independently.

The single summed score (dichotomized as less than or equal to 14 vs greater than 14) has been reported in several prospective cohort studies about the validity of the FMS to predict musculoskeletal injury (Table 2)^[22-30]. Most of the studies reported low sensitivity^[22-24,26,29] that is the proportion of the sample who sustained an injury with a score less than or equal to 14 (approximately 50%). This means an equal proportion of the sample who sustained an injury scored above 14 or 14 or less. These studies had a variety of injury

definitions and studied samples, including professional and collegiate athletes, and military personnel. Two studies^[25,28] reported sensitivity above 70%. Hotta *et al.*^[28] studied 84 competitive male runners, and with an injury definition of a training related injury resulting in time loss for 4 wk, the sensitivity of the dichotomized FMS score to predict injury was 73%. Butler *et al.*^[25] reported a sensitivity of 84% for the dichotomized FMS score and injuries related to training and requiring 3 consecutive days of missed training in 108 firefighter trainees. Therefore, perhaps the FMS is more sensitive for predicting more serious injuries requiring time loss from training, although other studies with this injury definition reported low sensitivity^[22,24]. The specificity, or the proportion of the studied samples who did not sustain an injury with a FMS score greater than 14 was far more varied, ranging from 46%^[26] to 91%^[22], so it is difficult to make any definitive conclusions about the specificity. It is evident that there is not a consensus on the ability of the FMS as a single score to predict injury. Part of this is due to the differing samples studied and injury definitions used, as well as the recent studies pointing to the caution with a single FMS score^[20,21]. Additionally, several studies reported an inability to find a point on the receiver operator characteristic (ROC) curve that maximized sensitivity and specificity for the studied sample^[24,26], and defaulted to 14 as a cut-point based on previously published literature.

Three of the aforementioned studies prospectively assessed the association of each movement pattern with injury^[25,26,28]. Butler *et al.*^[25] reported a significant association between 3 d time loss injuries and deep squat (OR = 1.21; 95%CI: 1.01-1.42) and push-up (OR = 1.30; 95%CI: 1.07-1.53) and Hotta *et al.*^[28] reported a significant association between 4 wk time loss injury and deep squat and active straight leg raise analyzed together (OR = 9.7; 95%CI: 2.1-44.4). Conversely, Warren *et al.*^[26] found no significant association between individual movement patterns and injury. It is obvious that further work is required to determine the validity of the FMS to predict injury, either as a summed single score, or perhaps more appropriately as individual movement patterns.

Finally responsiveness, or the ability of an instrument to accurately detect change when it has occurred^[31] is closely related to validity and informs the accuracy of an instrument. The ability of the FMS to improve in response to an intervention has been reported in 4 studies of 3 samples^[32-35]. In both American football players ($n = 62$)^[35] and mixed martial arts athletes ($n = 25$)^[32], an intervention of corrective exercise was designed based on baseline FMS scores. After 7 wk, the American football players improved the FMS overall score by approximately 3 points ($P < 0.001$) and had a significant decrease in the number of participants with asymmetrical movements with the 5 bilateral FMS movement patterns ($P = 0.01$)^[35]. Bodden *et al.*^[32] compared an 8 wk intervention program to a control group and reported a significant time by group

interaction ($P < 0.001$). The intervention group improved overall FMS score by approximately 2 points compared with no change in the control group. The change score reported in both of these studies appears to be consistent with a proposed Minimally Clinically Important Difference of 1.25 for the FMS score^[13]. Conversely, a study in 60 firefighters comparing 2 different interventions with a control group found no significant changes in FMS score after a 12 wk intervention ($P = 0.18$)^[33,34]. Additionally, no difference in number of participants with asymmetry was found ($P = 0.53$).

Despite the popularity, the evidence for the FMS is conflicting, limiting the ability to make definitive recommendations for use. It is a reliable instrument and clinicians should feel comfortable with the consistency of the scoring criteria. Caution should be exercised in using a single summed FMS score or a specific cut-point for injury. As an injury prediction screen, the validity was most accurate with firefighters^[25], but firefighters' scores were not responsive to an exercise intervention designed to prevent injury^[33,34]. American football players' scores were very responsive to an intervention^[35], and despite low sensitivity an FMS score 14 or less was significantly associated with time loss injuries (OR = 1.87; 95%CI: 1.20-2.96)^[36]. Additionally, two studies have failed to show a significant difference in FMS scores between injured and uninjured^[25,37]. Although there have been over 60 papers published on the accuracy and use of the FMS in the last 5 years, the only clear conclusions are that the FMS is reliable and appears to have good utility in professional American football players as a single summed score. Although this editorial included studies on adults only, there have been a number of studies recently published on the use of FMS in adolescents. Further work is required here to determine if the similar findings occur in adolescents compared with adults.

STAR EXCURSION BALANCE TEST/Y BALANCE TEST

The Star Excursion Balance Test (SEBT) (Figure 2) was first described in the literature for research purposes more than 15 years ago^[38]. Since this time a PubMed search shows that approximately 150 publications have utilized this tool for assessing dynamic balance across numerous populations. The SEBT assesses dynamic single leg balance while reaching in 8 reach directions based on the orientation of the stance limb: Anterior, posterior, medial, lateral, anterior lateral, anterior medial, posterior lateral, and posterior medial. The SEBT was first suggested to be modified based on redundancy, as a result of large amount of shared variance, across the 8 reaching directions; this was identified through a factor analysis of SEBT performance in participants with chronic ankle instability^[39]. This led to the suggestion of three reach directions, anterior, posterior medial, and posterior lateral rather than

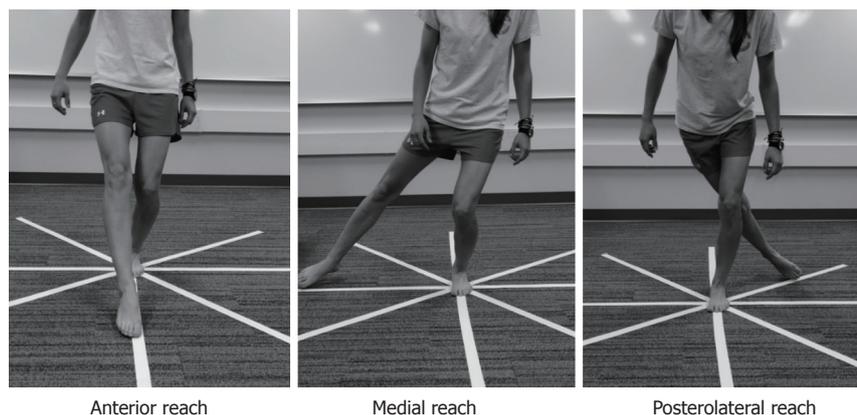


Figure 2 Images of the Star Excursion Balance Test.

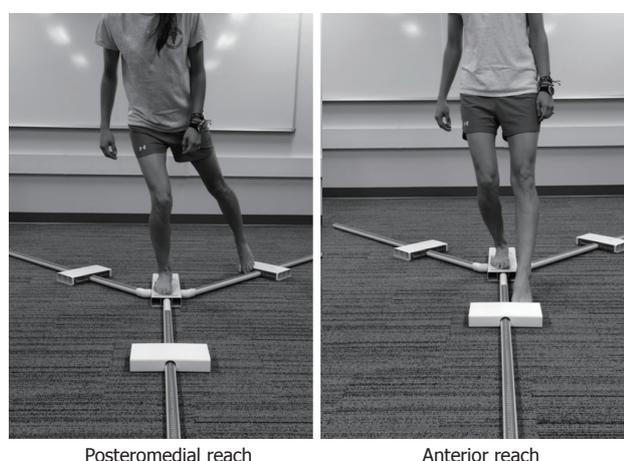


Figure 3 Images of Y Balance Test.

needing to perform all eight from the original SEBT^[40].

The SEBT is performed by placing strips of tape on the floor in a grid format while the participant stands in the middle of the grid and reaches as far as possible in one reach direction touching down lightly so the researcher can mark and subsequently measure the reach distance. Trials are considered successful when there is no movement in the stance limb during performance of the SEBT, controlled motion while maintaining balance, and returning of the reaching limb back to the starting point^[39]. The Y Balance Test (YBT) (Figure 3), an instrumented, proprietary version of the modified three reach SEBT, first appeared in the literature in 2009 with the intent of improving test repeatability^[41]. This device is made of PVC piping and has a center platform the participant stands on while reaching with the contralateral limb and lightly pushing a reach indicator as far as possible along a PVC piping tube. Scoring for both the modified SEBT and YBT involve determining the farthest reach in each of the three reach directions (anterior, posteromedial, and posterolateral) and creating a normalized composite reach score (CS), a normalized single direction reach, and/or a single reach direction asymmetry measurement. The normalized (by participant's leg length) reach distance has been

recommended for comparison because performance differences may be a result of anthropometric characteristics^[42]. The normalized CS, expressed as a percent, is calculated by averaging the maximum reach in each of the three reach directions, dividing this number by 3 times leg length (LL)^[43]. The normalized single reach direction is also expressed as a percent, and is calculated by taking the maximum reach in the single reach direction, dividing this number by LL^[42]. The single reach direction asymmetry measurement is calculated as the absolute difference in centimeters between the right and left limb for a single reach direction^[43].

A review of the literature suggests that inter-rater reliability of the YBT is slightly higher than the SEBT for the normalized reach distances [ICC 0.99-1.00 (95%CI: 0.92-1.0)^[41] vs 0.89-0.94 (95%CI: 0.80-0.95)]^[44] and the CS [ICC range 0.97-0.99 (95%CI: 0.92-0.99)^[41] vs 0.92 (95%CI: 0.85-0.96)]^[42]; it should be noted that both the YBT and SEBT have very good inter-rater reliability. Intra-rater reliability appears similar between the YBT normalized reach directions [ICC range = 0.85-0.91 (95%CI: 0.64-0.95)]^[41] and the SEBT (ICC range = 0.84-0.92; 95%CI: not reported)^[45]. For the YBT CS, Plisky *et al*^[41] reported intra-rater reliability to be high (0.91 95%CI: 0.69-0.96); however, Munro *et al*^[45] did not report the ICC for the SEBT CS; therefore, a direct comparison of intra-rater reliability for the CS cannot be made between the YBT and SEBT.

While it appears that using an instrumented device to measure dynamic balance (*i.e.*, YBT), may have a higher overall reliability, there is one main difference in the protocols between the YBT^[41] and SEBT^[38]. The YBT allows for stance foot movement during performance of dynamic reaching. Although this may seem like a subtle difference in protocol, there have been two studies to date that have found differences in performance and kinematics during a direct comparison of the YBT and SEBT performance^[46,47]. Participants reached further in SEBT anterior reach compared to YBT anterior reach^[46]; while utilizing less hip flexion^[47]. The development of the YBT was based on the SEBT; however, differences in performance may suggest that these two tests are not as similar as previously thought and that there needs to

be more research to assess neuromuscular differences between these two dynamic balance tools before assuming that findings from the SEBT translate to the YBT.

The normalized reach distance, composite score, and reach distance asymmetry may seem like reasonable means for comparing the SEBT and YBT performance, little attention has been dedicated to the validity of these measurements. In fact, a factor analysis has yet to be performed. Interestingly, dynamic balance differences have been noted between sexes^[13,48], ages^[49], countries of origin^[50], sport participation^[51], and sport level^[52]. Further, Lehr *et al.*^[53] assessed risk of noncontact injury based on YBT performance in 183 Division III athletes from 10 NCAA sports teams and recommended that injury risk should be based on sport, sex, and age.

Despite the numerous publications involving the use of the SEBT and the YBT, there are only 4 published studies that have used one of these tools to determine sport injury risk. In a study on lower extremity non-contact injury risk in high school athletes, Plisky *et al.*^[43] demonstrated that a CS of less than 94% LL resulted in a 6.5 times greater odds (95%CI: 2.4-17.5) of lower extremity injury female high school athletes and an anterior reach asymmetry of more than 4cm resulted in a 2.7 times greater odds (95%CI: 1.4-5.3) of lower extremity injury in all high school athletes ($n = 235$; 30 boys, 105 girls). Butler *et al.*^[54] found that lower extremity noncontact injury risk was 3.5% higher (95%CI: 2.4-5.3) in collegiate Division III football players ($n = 59$) with a CS of less than 89.6% LL. In this study ROC analysis revealed that a composite score 89.6% LL maximized sensitivity (100%) and specificity (71.7%); however, ROC analysis of reach asymmetry did not find an ideal cut point for identifying injury risk^[54]. Conversely, Smith *et al.*^[55] also used the YBT to assess risk of injury based on YBT performance in 184 Division I athletes from 13 NCAA sports teams and found that noncontact injury was associated with 4 or more cm of anterior reach asymmetry (OR = 2.33; 95%CI: 1.15-4.76). This study used an ROC curve and determined that 4 cm was the optimal cut point (sensitivity: 59%; specificity: 72%) for predicting injury; interestingly, ROC curve failed to maximize sensitivity and specificity for composite score; there was no relationship between CS and injury^[55]. Lastly, Olivier *et al.*^[56] found no difference in SEBT composite score between cricket pace bowlers who sustained lower extremity injury and those that did not ($n = 32$, 17 injured-left leg: 79.65% LL vs 83.26% LL; $P = 0.16$; right leg: 78.70% LL vs 81.59% LL; $P = 0.18$); however, those who were injured performed significantly worse on the normalized posteromedial reach direction than those who were not injured (90.07% LL vs 91.26% LL; $P = 0.02$). In this study of cricket pace bowlers all injuries that resulted in time loss of at least one day or required the bowler to quit activity in which they had already started was included; this implies that all injuries were included rather than

just non-contact injuries. Additionally, the authors did not report reach asymmetry differences in this study, which combined with the inclusion of all injuries, makes comparison between this and previous studies difficult. It should be noted that the CS in the cricket bowling study^[56] were lower than those reported in the previous studies in which noncontact injury was associated with CS performance of lower than 94%^[43] or 89.6%^[54].

To date 7 studies have evaluated the effects of dorsiflexion range of motion^[57,58], sex and injury history^[13], and interventions on SEBT/YBT performance^[59-62]. Forty-five individuals (12 males; 33 females with chronic ankle instability and reduced dorsiflexion range of motion had significant, but low positive correlations with performance on the SEBT CS ($r = 0.30$, $r^2 = 0.09$, $P = 0.02$) and normalized anterior ($r = 0.55$, $r^2 = 0.31$, $P < 0.001$) and posterolateral ($r = 0.29$, $r^2 = 0.09$, $P = 0.03$) reach^[57]. Further, Hoch *et al.*^[58] reported that dorsiflexion range of motion as measured by the weight bearing lunge test ($n = 35$; 14 males; 21 females) explained 28% of the variance in the normalized anterior reach of the SEBT leading the authors to suggest that the anterior reach of the SEBT may be a good test to determine the effects of dorsiflexion limitations on dynamic balance performance. While it does not appear that males ($n = 103$) and females ($n = 87$) perform differently on YBT CS (102% \pm 8% vs 100% \pm 6%; $P = 0.05$), males have been reported to have a significantly greater anterior reach asymmetry compared to females (4.4 \pm 6.7 cm vs 2.7 \pm 2.3 cm; $P = 0.02$)^[13]. Additionally, one study indicated that history of injury or surgery did not affect YBT CS or asymmetry; however, those who reported a back or trunk injury had greater variability in asymmetry in the anterior and posterior medial reach directions^[13]. This finding is particularly interesting as trunk stability exercises (front plank, quadruped, and back bridges) have been demonstrated to provide immediate improvement in normalized SEBT CS (94.0% \pm 4.8% vs 96.8% \pm 5.7%; $P < 0.001$) and posterolateral (102.8% \pm 7.3% vs 106.2% \pm 8.1%; $P = 0.002$) and posteromedial (105.3% \pm 5.8% vs 109.8% \pm 6.4%; $P < 0.001$) reach directions ($n = 11$)^[59]. Additionally, after 12 wk of trunk stability exercises, 27 soccer players demonstrated improvement in normalized posteromedial (101.5% \pm 7.2% vs 110.0% \pm 9.3%; $P = 0.013$) and posterolateral (96.2% \pm 12.9% vs 104.7% \pm 8.1%; $P = 0.02$)^[60]; while an 8 wk lower extremity neuromuscular training program focused on core stability and lower extremity strength improved SEBT CS (right: Pre-training-96.4% \pm 11.7% vs post-training-104.6% \pm 6.1%; $P = 0.03$; left: Pre-training-96.9% \pm 10.1%; post-training: 103.4% \pm 8.0%; $P = 0.04$) in 20 uninjured soccer players (13 experimental; 7 control)^[61]. Interestingly, Ambegaonkar *et al.*^[63] found that hip strength, rather than core endurance (McGill's Core Endurance Tests), was associated with SEBT performance in 40 collegiate female lacrosse and soccer athletes. Additionally, Garrison *et al.*^[62] reported a significant decrease in



Figure 4 Images of the Drop Jump Screening Test. Participants drop off of the box and upon landing on the ground they are asked to immediately explode up in to a vertical jump. Image is at max height of vertical jump.

anterior reach asymmetry tested with the YBT in participants with ACL reconstruction after 12 wk of a traditional rehabilitation plus isolated hip strengthening rehabilitation ($n = 22$) compared to those in traditional rehabilitation ($n = 21$) only (2.7 ± 2.9 vs 6.1 ± 4.6 ; $P = 0.008$).

These differences between groups and studies may suggest the types of analytic comparisons currently being conducted to determine differences between groups when performing the YBT/SEBT may not fully capture the risk of injury attributable to dynamic balance performance. In taking into consideration all of the studies presented here it appears that anterior reach asymmetry is most affected in terms of sex differences and dorsiflexion range of motion; while core training appears to help mitigate performance differences. Additional research is needed in regards to the CS as there are differences in the maximized cut-point to use for injury prediction; however anterior reach asymmetry of 4 or more cm appears to consistently predict non-contact injury risk. It is also important to consider that there are a number of factors that contribute to dynamic balance performance and thus may need to be accounted for when assessing injury risk based on lower extremity dynamic balance.

DROP JUMP TEST

The Drop Jump Test (Figure 4) has been described in the literature as a tool to evaluate landing patterns from a clinical perspective using either the DJST or the LESS.

DJST

The DJST is a clinical used to assess dynamic knee valgus on landing from a 30.48 cm height and immediately exploding into a vertical jump *via* a simple frontal plane video analysis of normalized knee joint separation distance (calculated as knee separation distance/hip separation distance); it was first described in the literature approximately 10 years ago^[64]. This tool was designed based on the group's prior work^[65], which assessed landing mechanics in youth athletes^[64]. This test uses reflective markers placed bilaterally on the greater trochanter, center of the patella, and lateral malleolus to determine differences in hip, knee,

and ankle joint separation during three phases of the drop jump: Pre-landing, landing, and take-off. At the completion of three jumps, the researcher chooses the best representative jump and analyzes the jump frame by frame to identify the pre-landing, defined as the frame when the athlete's toes just touch the ground after the jump from the box, the landing, defined as the frame in which the athlete has the greatest amount of knee flexion, and the take-off, defined as the frame in which there is initial upward movement to initiate the vertical jump^[64]. For each of the three identified frames listed previously, the researcher uses a proprietary software (Valgus Digitizer, Sportsmetrics™ Software for Analysis of Jumping Mechanics, Cincinnati, OH) to digitize the marker points; from the digitized points the software computes absolute difference between right and left hips and normalized difference between right and left knees (knee separation distance/hip separation difference) and ankles (ankle separation distance/hip separation difference)^[64]. Less than 60% normalized knee joint separation is representative of abnormal frontal plan knee valgus alignment^[64].

Three studies^[64,66,67] have evaluated sex differences in the DJST with one documenting no difference between females and male in normalized knee separation distance at landing ($51\% \pm 19\%$ vs $51\% \pm 15\%$; $P > 0.05$) and take-off ($50\% \pm 18\%$ vs $53\% \pm 15\%$; $P > 0.05$); however, females demonstrated higher normalized knee separation distance than males during the pre-landing phase ($63\% \pm 14\%$ vs $59\% \pm 11\%$; $P < 0.0001$)^[64]. Barber-Westin *et al*^[66] also demonstrated no differences in normalized knee separation distance between sexes across various age groups from 9-17 years of age. In another study of a similar population, females had significantly lower knee-hip ratio (0.45 vs 0.63 ; $P = 0.003$) (standard deviations were not reported)^[67].

In the inaugural study^[64] using the DJST to analyze knee joint separation as a means for defining dynamic knee valgus the authors reported the tool is reliable as demonstrated in the following. On a subset of 17 participants who underwent a second DJST 7 wk after the first screening hip joint separation reliability was assessed to provide support for the normalized differences. The authors also presented a subset of another 10 participants in which 2 of the 3 trials were

Table 3 Landing Error Scoring System scoring criteria

LESS item	Operational definition of error
Knee flexion: Initial contact	Knee is flexed less than 30° at initial contact
Hip flexion: Initial contact	Thigh is in line with the trunk at initial contact
Trunk flexion: Initial contact	Trunk is vertical or extended on the hips at initial contact
Ankle plantar flexion: Initial contact	Foot lands heel to toe or with flat foot at initial contact
Medial knee position: Initial contact	Center of patella is medial to midfoot at initial contact
Lateral trunk flexion: Initial contact	Midline of trunk flexed to left/right side body at initial contact
Stance width: Wide	Feet positioned > shoulder width apart at initial contact
Stance width: Narrow	Feet positioned < shoulder width apart at initial contact
Foot position: External rotation	Foot is internally rotated more than 30° between initial contact and maximum knee flexion
Foot position: Internal rotation	Foot is externally rotated more than 30° between initial contact and maximum knee flexion
Symmetric initial foot contact	One foot lands before other or one foot lands heel to toe and other lands toe to heel
Knee flexion displacement	Knee flexes less than 45° between initial contact and max knee flexion
Hip flexion displacement	Trunk does not flex more on trunk between initial contact and maximum knee flexion
Trunk flexion displacement	Trunk does not flex more between initial contact and maximum knee flexion
Medial knee displacement	At maximum medial knee position, the center of patella is medial to midfoot
Joint displacement	Soft: Participant demonstrates large amount of trunk, hip, and knee displacement Average: Participant has some but not large amount of trunk, hip, and knee displacement Stiff: Participant goes through very little, if any, trunk, hip, or knee displacement
Overall impression	Excellent: Participant displays soft landing with no frontal or transverse plane motion Poor: Participant displays large frontal or transverse plane motion, or participant displays stiff landing with some frontal or transverse plane motion Average: All other landings

Flaws 1-15 scored as present: 1 and absent = 0; Flaw 16 scored as soft: 0, average = 1, stiff = 2; Flaw 17 scored as excellent: 0, average = 1, poor = 2. LESS: Landing Error Scoring System.

tested for reliability of absolute separation of the hip, knee, and ankle. The ICCs for hip joint separation were reported as very high at pre-landing (0.96), landing (0.94), and take-off (0.94). The ICCs for absolute separation of the hip, knee, and ankle were reported as all being ≥ 0.90 .

Several studies have been published evaluating the effects of neuromuscular training program on the DJST; however, all studies have arisen from the same research group. Further, the validity of such a measurement (knee joint separation) to indicate dynamic knee valgus has never been established. In response to the validity of the DJST, Dr. Noyes and Ms. Barber-Westin state in a Letter to the Editor^[68] that "our investigations show the dramatic differences (in landing appearance) between knees with $\leq 60\%$ and those with $> 60\%$ normalized knee separation distance". While this does not actually demonstrate that the DJST is a valid measure, there are documented improvements in knee joint separation following neuromuscular training programs in a variety of different athletes^[69-71].

Thirty-four female high school volleyball players took part in a 6 wk sport specific neuromuscular training program, which resulted in significant increases in absolute knee separation (21.1 ± 8.2 cm vs 25.9 ± 5.2 cm; $P = 0.002$) and mean normalized knee separation distance ($56.3\% \pm 19.1\%$ vs $63.3\% \pm 12.7\%$; $P = 0.04$)^[69]. Sixty-two female high school soccer player participated in a 6 wk sport specific neuromuscular training program and had post training increased ankle (27.3 ± 6.3 cm vs 34.6 ± 6.0 cm; $P < 0.0001$) and knee (14.6 ± 3.6 cm vs 23.1 ± 24.7 cm; $P < 0.0001$) absolute separation distance and normalized

knee separation distance ($35.9\% \pm 7.4\%$ vs $54.2\% \pm 13.7\%$; $P < 0.0001$) when completing the DJST^[71]. Fifty-seven female high school basketball players demonstrated increased absolute knee separation (18.5 ± 7.4 cm vs 31.8 ± 10.4 cm; $P < 0.0001$) and mean normalized knee separation distance ($44.9\% \pm 17.2\%$ vs $74.2\% \pm 18.8\%$; $P < 0.0001$) following 6 wk of neuromuscular training^[70]. Based on the previous suggestion that less than 60% normalized knee separation distance indicating dynamic knee valgus^[64]; these findings suggest that a more neutral knee alignment was achieved at landing following the sport specific neuromuscular training programs in female high school volleyball, soccer, and basketball athletes. Additionally, improvements in landing alignment were maintained at 12 mo after a 6 wk neuromuscular training program in approximately 70% of female volleyball players^[72]. It is important to note that although the results of the aforementioned studies suggest that landing alignment may be altered following a specific training program; there remains a lack of literature on the validity of the DJST and to date this screening tool has not been used to predict injury risk.

LESS

The LESS is similar to the DJST in the test procedures with the exception that participant's jump landing is video recorded from both the frontal and sagittal planes. In addition, when performing the drop jump landing for the LESS, participants jump from a 30-cm height jump to land on the floor at a distance that is 50% of their height away from the box and then immediately perform a maximal vertical jump. In the LESS, which

Table 4 Landing Error Scoring System scoring criteria real-time

LESS RT item	Operational definition	View	Jump number
Stance width	Participant lands with very wide or very narrow stance (+1)	Front	1
Maximum foot-rotation position	Participants feet moderately externally or internally rotated at any point during the landing (+1)	Front	1
Initial foot-contact symmetry	One foot lands before the other or 1 foot lands heel-to-toe and other foot lands toe-to-heel (+1)	Front	1
Maximum knee-valgus angle	Participant moves into a small amount of knee valgus (+1); Participant moves into a large amount of knee valgus (+2)	Front	2
Amount of lateral trunk flexion	Participant leans to left or right so trunk is not vertical in the frontal plan (+1)	Front	2
Initial landing of feet	Participant lands heel to toe or with flat foot (+1)	Side	3
Amount of knee-flexion displacement	Participant goes through small (+2) or average (+1) amount of knee flexion displacement	Side	3
Amount of trunk-flexion displacement	Participant goes through small (+2) or average (+1) amount of trunk flexion displacement	Side	4
Total joint displacement in sagittal plane	Participant goes through large displacement of trunk and knees, score soft (0); Participant goes through average displacement of trunk and knees, score average (+1); Participant goes through minimal displacement of trunk and knees, score stiff (+2)	Side	All
Overall impression	Participant displays soft landing and no frontal plane motion at knee, score excellent (0); Participant displays stiff landing and large frontal plane motion at knee, score poor (+2); All other landings score average (+1)		

LESS: Landing Error Scoring System.

Table 5 i-Landing Error Scoring System criteria

Good movement pattern	Poor movement pattern
Lands with no knee valgus at initial foot contact	Lands with moderate to large knee valgus position at initial foot contact
Lands with no knee valgus displacement from initial contact to maximum knee flexion	Lands with moderate to large knee valgus displacement from initial contact to maximum knee flexion
Lands with > 30° of knee flexion	Lands with < 30° of knee flexion
Undergoes > 30° of knee flexion	Undergoes < 30° of knee flexion from initial contact to full knee flexion
Minimal to no sound upon landing	Loud sound upon landing

was first described in the literature approximately 6 years ago^[73], participants are scored offline *via* a 17 item clinical tool evaluating "landing error" (Table 3) to identify movement patterns that lead to increased ACL injury risk. Newer studies demonstrate the use of real time scoring of four jumps using a modified version of the LESS (LESS-RT) with the scorer evaluating 10 errors during 4 participant jumps (Table 4)^[74] and real time scoring using a single jump and the iLESS scoring (Table 5)^[75].

The LESS demonstrated good to excellent reliability and was validated against the gold standard of three dimensional kinematic and kinetic analysis in a large study involving approximately 2700 military academy attendees^[73]. Intra- (ICC = 0.91) and inter-rater (ICC = 0.84) reliability were established using a random subset of 50 from the initial study; concurrent validity was established by demonstrating that those participants with low LESS scores demonstrated less knee and hip flexion angle, increased knee valgus and hip adduction angle, increased internal knee and hip internal rotation moment, and anterior tibial shear force^[73]. The importance of this work is that the authors demonstrated that a clinical movement screen can be used to identify landing errors in multiple planes. Further work has established that the LESS can be used by both novice and expert LESS raters with excellent reliability (overall score: ICC = 0.84; kappa

statistics for individual items/landing errors ranged from 80%-100% agreement); however, the validity of the LESS (compared to 3 dimensional motion analysis) is dependent on the item/error being assessed based on Phi-correlation-coefficient analysis leading the authors to suggest that items/errors not valid should be reduced or eliminated from the LESS scoring criteria^[76]. To enhance the utility of the LESS, the LESS-RT was developed and the reliability of the composite score (total of 10 errors) was assessed as being good both for interrater reliability (ICC = 0.81)^[74]. To create a more efficient clinician screening tool, the iLESS was developed and allows for quicker assessment of large groups in a short amount of time, like a pre participation examination, and demonstrated a high level of agreement between novice and expert raters (iLESS: Kappa = 0.692, Agreement = 90%, $P = 0.001$; LESS: Kappa = 0.600, Agreement = 80%, $P = 0.001$) and with the LESS (novice: Kappa = 0.583, Agreement = 85%, $P = 0.004$; expert: Kappa = 0.500, Agreement = 75%, $P = 0.01$)^[75].

Performance of the LESS is influenced by sex^[77,78], fatigue^[79], and previous ACL reconstruction^[79-81]. In a large study of over 200 collegiate athletes, Lam *et al.*^[77] found that while males and females demonstrate similar overall LESS scores statistically, males performed worse on items 1, 4, 14 and females performed worse on items 5 and 15 and had more overall frontal plane movement and total errors. This study suggested that

Table 6 Technique flaws of the Tuck Jump Assessment

Lower extremity valgus at landing
Thighs do not reach parallel (peak of jump)
Thighs not equal side-to-side (during flight)
Foot placement not shoulder width apart
Foot placement not parallel (front to back)
Foot contact timing not equal
Excessive landing contact noise
Pause between jumps
Technique declines prior to 10 s
Does not land in same footprint (excessive in-flight motion)

males demonstrate more sagittal plane landing errors while females display more frontal plane landing errors. Beutler *et al.*^[78] reported that females cadets had lower overall LESS scores compared to male counterparts (5.34 ± 1.51 vs 4.65 ± 1.69 ; $P < 0.001$); this study of 2753 participants also completed a factor analysis and determined that there are five groups of related errors: Factor 1: Knee (item 1), decreased hip (item 2), and trunk flexion (item 3) at initial contact; Factor 2: Knee valgus (item 5 and 15) and wide stance at initial contact (item 7); Factor 3: Toe out (item 10) and knee flexion at initial contact (item 1); Factor 4: Heel-to-toe landing (item 4) and asymmetric foot landing pattern (item 11); Factor 5: Reduced sagittal plane flexion during the landing phase (items 12, 13, and 14)^[78]. T-tests between male and females suggested that females are significantly more likely to present with Factors 1, 2, and 5 ($P < 0.001$), while males had greater likelihood of Factors 3 and 4 ($P < 0.001$)^[78]. Although not directly tested, the authors suggested that perhaps fatigue worsens movement patterns, which was validated by Gokeler *et al.*^[79] who demonstrated that after a fatigue protocol in participants with anterior cruciate ligament reconstruction (ACLR) and controls (no ACLR) performed worse on LESS total score compared to pre fatigue scores [median 7.0 (IQR: 4.3; 7.8) vs 5.0 (IQR: 2.0; 7.0); $P = 0.001$]. This study also assessed frequency of errors and found that post fatigue ACLR had a greater percentage of errors than control in knee flexion at initial contact, extension on the hips, lateral trunk flexion, and asymmetrical foot contact although the article did not state if these were significant differences^[79]. Similarly, Kuenze *et al.*^[80] and Bell *et al.*^[81] demonstrated that ACLR have significantly lower total LESS scores than healthy controls (6.0 ± 3.6 vs 2.8 ± 2.2 ; $P = 0.002$ and 6.7 ± 2.1 vs 5.6 ± 1.5 ; $P = 0.04$, respectively).

Recent evidence suggests that the LESS can be modified through training^[82-84] and it can also be used to identify those at risk for injury^[85,86]. Following completion of a military course designed to improve performance in military tasks, cadets had significant improvement in LESS scores (5.01 ± 1.83 vs 4.48 ± 1.97 ; $P < 0.001$)^[81]. Similarly, completion of an 8 wk program including progressive resistance exercise and core stability, power, and agility exercises participants performed better on the

LESS compared to those who participated in a program that consisted of progressive resistive upper and lower extremity exercises only (pretest: 3.90 ± 1.02 , posttest: 3.03 ± 1.02 ; $P = 0.02$)^[83]. However, length of training appears to impact retention of improved performance on the LESS as participants taking part in 9 mo of training maintained movement pattern changes after 3 mo of no training while those that participated in 3 mo of training did not^[84].

A very recent report suggests that LESS scores can be used to predict ACL injury risk^[85]; however, this is in contradiction to a slightly older study in which LESS scores were unable to predict ACL injury^[86]. Smith *et al.*^[86] was unable to determine a relationship between ACL injury risk and LESS score in a large study of over 5000 collegiate and high school athletes (OR = 1.04 per unit increase in LESS score; 95%CI: 0.80-1.35). Padua *et al.*^[85], however, was able to identify through ROC analysis that the optimal cut-point for LESS scoring as a predictor of ACL injury was 5.17 (sensitivity: 86%, specificity: 71%) using a sample of 829 youth elite soccer players. Athletes who sustained ACL injury had higher LESS scores than those that did not (6.24 ± 1.75 vs 4.43 ± 1.71 ; $P < 0.005$) and those athletes who had a LESS score of 5 or more had a 10.7 greater risk ratio than those who scored less than 5^[85].

The LESS is a reliable tool that appears to have validity although caution should be taken as there may be some items/errors that are not completely validated. Clinicians should account for sex, fatigue, and previous ACLR as these all have demonstrated effects on LESS performance. Further, various types of training programs may improve LESS performance, which may influence ACL injury rate although more studies are warranted at this point.

TJA

The TJA (Figure 5) is a clinical test developed to identify lower extremity landing technique flaws during a plyometric activity^[87,88]. The TJA is a quick (10 s) assessment of repetitive tuck jump performance, requiring a high level of effort, which may result in fatigue. The TJA is video recorded in the sagittal and frontal plane and is scored from the recording allowing assessment in slow motion and repeated viewings. There are 10 technique flaws (Table 6) scored as either present or absent during the TJA^[87,88].

The benefits of the TJA are that it is a quick, inexpensive, and easy to administer. Two off-the-shelf video camera, tripods, and marking tape are all that is required to complete this test. The cameras must allow full visualization of the trunk and lower extremities with jumping and landing, so this test can be completed with minimal space requirements (8' x 8'). The TJA takes no more than 2 min to administer, and no more than 10 min to score, making this a viable option for many.

There is limited literature published on the TJA (the 10 s test). A PubMed search using the search terms

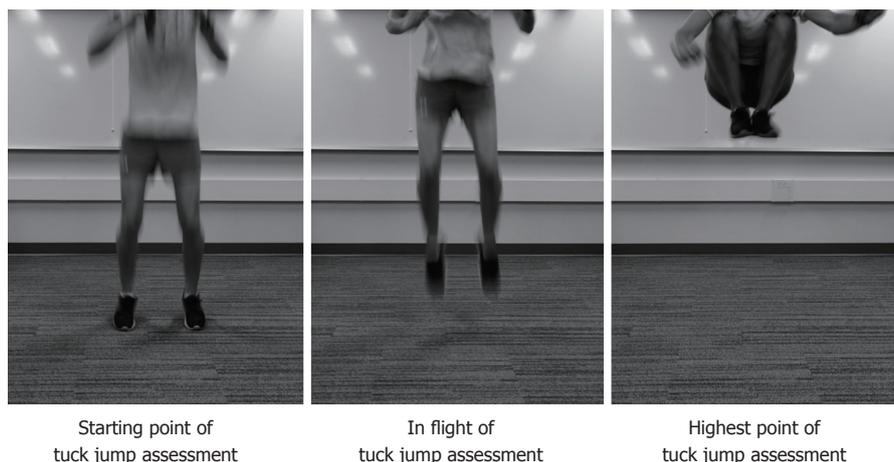


Figure 5 Images of the Tuck Jump Assessment.

(“tuck jump assessment” OR “tuck jump”) yielded only 7 results that included the TJA. Despite the lack of evidence, this assessment is widely used clinically based on anecdotal information from PTs, ATs, and performance specialists.

There are 3 studies assessing the reliability of the TJA. The first assessed a different version of the scoring of the TJA^[89]. A continuous 10 cm scale was used for 8 technique flaws and reported an intra-rater reliability correlation of 0.84 (range 0.72 -0.97). The TJA scoring was modified to dichotomize the technique flaws (10 rather than the initial 8) to enhance reliability^[87], and is the test used in the 2 more recent TJA reliability articles^[90,91]. Two raters (including 1 of the developers of the TJA) initially examined inter- and intra-rater reliability in 10 participants 1 mo apart^[90]. Excellent inter-rater reliability was reported with high percentage exact agreement (PEA) between the 2 raters (93%, range 80%-100%) and Kappa of 0.88 indicating good/excellent agreement. Intra-rater reliability was also excellent with PEA 96% and 100% for the 2 raters for male participants and average of 87.2% for female participants. Both of these raters are experts and highly educated in movement science, and one of the raters developed the test. Therefore, these excellent results may not generalize to the variety of clinicians who employ the TJA. We examined inter- and intra-rater reliability in 40 participants using 5 raters of different educational backgrounds and clinical experience (PT and PT students, AT, and strength and conditioning coach)^[91]. All raters were given instructions, Myer *et al.*^[88] that describes the TJA and scoring in detail, as well as a scored, example TJA previously scored and consensus achieved by the researchers. Inter-reliability between the 5 raters was poor (ICC = 0.47; 95%CI: 0.33-0.62). Incidentally, the 3 raters who completed the intra-rater reliability improved the inter-rater reliability on the second scoring 1 wk later (ICC = 0.52; 95%CI: 0.35-0.68 for scoring 1 vs ICC = 0.69; 95%CI: 0.55-0.81). This improvement in consistency amongst raters may be due to a learned effect with the

scoring criteria. Intra-rater ICC (95%CI) was varied for the 3 raters, ranging from 0.44 (0.22-0.68) to 0.72 (0.55-0.84). Surprisingly, the most consistent rater was a 1st year PT student with very little experience in movement analysis. The difference in reliability between these 2 studies highlights the need for more research on TJA for consistent use clinically.

The validity of the TJA has not been formally assessed. Again, the face validity is unquestioned as the developers are movement specialists and have an extensive body of literature on lower extremity biomechanics published from the lab^[88,92-94]. Furthermore, Myer *et al.*^[88] presented a categorization of the 10 TJA technique flaws into five different modifiable risk factors: Ligament dominance, quadriceps dominance, leg dominance or residual injury deficits, trunk dominance (“core” dysfunction), and technique perfection (Table 7). Biomechanical research provided some support for these risk factor categorizations^[94], but this has not been assessed clinically or statistically. The responsiveness was also recommended that anyone with 6 or more flaws should be targeted for preventive intervention^[88], but no data were presented to justify that recommendation.

The TJA has not been compared with other clinical jumping assessments, but there may be some advantages of the TJA compared with the DJST, which requires a participant to jump off a 30.48 cm box, land, and immediately perform a maximal vertical jump^[95]. Because this screening tool involves the use of markers it has a slightly more involved set up. The TJA is also advantageous over the LESS as the scoring for the LESS is more involved as a result of evaluating 17 landing technique errors (present or not) on “a range of readily observable items of human movement”^[73]. The TJA is a 10 s test vs the 1-2 jumps for other tests and may potentially allow measurement of performance endurance, and fatigue^[87]. Similar validation with the TJA is required to ensure the validity of the assessment. The TJA, unlike the other two tests, starts and stops from ground level instead of jumping from a box; this

Table 7 Categorization of 10 technique flaws from the Tuck Jump Assessment into modifiable risk factors

Modifiable risk factor	Description	Technique flaws
Ligament dominance	“Imbalance between the neuromuscular and ligamentous control of the dynamic knee stability”	Lower extremity valgus at landing Foot placement not shoulder width apart
Quadriceps dominance	“Imbalance between knee extensor and flexor strength, recruitment, and coordination”	Excessive landing contact noise
Leg dominance or residual injury deficits	“Imbalance between the 2 lower extremities in strength, coordination, and control”	Thighs not equal side-to-side (during flight) Foot placement not parallel (front to back) Foot contact timing not equal
Trunk dominance/core dysfunction	“Imbalance between the inertial demands of the trunk and core control and coordination to resist it”	Thighs do not reach parallel (peak of jump) Pause between jumps Does not land in same footprint (excessive in-flight motion)
Technique perfection	Not defined	Technique declines prior to 10 s

better represents techniques encountered in normal jumping activities.

None of these jumping assessments have been investigated as an injury prediction tool. All of these assessments were designed to better understand ACL injury, and it is well known that ACL injury are multifactorial, and the mechanism of non-contact ACL injury is multiplanar^[73,95], the inclusion of these clinically jumping assessments as a sole predictor for ACL injury is not recommended. Despite the minimal published literature on the TJA, one recommendation can be offered. For the most consistent results, a single clinician should score the TJA if using this to assess progress with an intervention. Further research on the validity is needed to advocate the further use of the TJA clinically.

CONCLUSION

This editorial focused on clinical movement screening tests as they have gained a lot of popularity in the clinical setting as a tool to predict injury and guide injury prevention programs/training. However, clinicians should be aware that various factors like sex differences, previous injury history, and sport participation can influence the accuracy of these screening tests. The validity of the FMS has been questioned and conflicting findings on injury prediction make recommendations for use difficult at this time. The SEBT/YBT appear to have some potential for injury prediction when assessing anterior reach asymmetry, but the CS is a little less clear as there are varying cut-points being identified for injury risk prediction. Additionally, the validity of the SEBT/YBT has yet to be established. It is of the authors opinion that, while both the SEBT and YBT are reliable tools, the YBT is easier to use from a clinician standpoint. The DJST, while proven to detect normalized knee separation differences following neuromuscular training, has yet to be validated or established as a tool to predict injury risk. The LESS appears to have recent potential as an injury predictor; however, results between the only two studies published conflict on this. Additionally, one study has suggested that the LESS may need to have irrelevant items/errors removed to improve validity. Finally, the TJA appeared to be reliable from early studies; however, a newer study suggests

that it may not be very reliable and scoring by a single clinician leads to more consistency. Additionally, this tool has yet to be validated or proven as an injury risk predictor.

REFERENCES

- 1 **Rechel JA**, Yard EE, Comstock RD. An epidemiologic comparison of high school sports injuries sustained in practice and competition. *J Athl Train* 2008; **43**: 197-204 [PMID: 18345346 DOI: 10.4085/1062-6050-43.2.197]
- 2 **Hootman JM**, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. *J Athl Train* 2007; **42**: 311-319 [PMID: 17710181]
- 3 **Fuller CW**, Ekstrand J, Junge A, Andersen TE, Bahr R, Dvorak J, Hägglund M, McCrory P, Meeuwisse WH. Consensus statement on injury definitions and data collection procedures in studies of football (soccer) injuries. *Br J Sports Med* 2006; **40**: 193-201 [PMID: 16505073 DOI: 10.1136/bjsm.2005.025270]
- 4 **Dick R**, Agel J, Marshall SW. National Collegiate Athletic Association Injury Surveillance System commentaries: introduction and methods. *J Athl Train* 2007; **42**: 173-182 [PMID: 21714302]
- 5 **Cook G**, Burton L, Hoogenboom B. Pre-participation screening: the use of fundamental movements as an assessment of function - part 1. *N Am J Sports Phys Ther* 2006; **1**: 62-72 [PMID: 21522216]
- 6 **Cook G**, Burton L, Hoogenboom B. Pre-participation screening: the use of fundamental movements as an assessment of function - part 2. *N Am J Sports Phys Ther* 2006; **1**: 132-139 [PMID: 21522225]
- 7 **Smith CA**, Chimera NJ, Wright NJ, Warren M. Interrater and intrarater reliability of the functional movement screen. *J Strength Cond Res* 2013; **27**: 982-987 [PMID: 22692121 DOI: 10.1519/JSC.0b013e3182606df2]
- 8 **Fox D**, O'Malley E, Blake C. Normative data for the Functional Movement Screen in male Gaelic field sports. *Phys Ther Sport* 2014; **15**: 194-199 [PMID: 24556034 DOI: 10.1016/j.ptsp.2013.11.004]
- 9 **Loudon JK**, Parkerson-Mitchell AJ, Hildebrand LD, Teague C. Functional movement screen scores in a group of running athletes. *J Strength Cond Res* 2014; **28**: 909-913 [PMID: 24662154 DOI: 10.1097/JSC.0000000000000233]
- 10 **Schneiders AG**, Davidsson A, Hörman E, Sullivan SJ. Functional movement screen normative values in a young, active population. *Int J Sports Phys Ther* 2011; **6**: 75-82 [PMID: 21713227]
- 11 **Teyhen DS**, Riebel MA, McArthur DR, Savini M, Jones MJ, Goffar SL, Kiesel KB, Plisky PJ. Normative data and the influence of age and gender on power, balance, flexibility, and functional movement in healthy service members. *Mil Med* 2014; **179**: 413-420 [PMID: 24690966 DOI: 10.7205/MILMED-D-13-00362]
- 12 **Perry FT**, Koehle MS. Normative data for the functional movement screen in middle-aged adults. *J Strength Cond Res* 2013; **27**: 458-462 [PMID: 22561971 DOI: 10.1519/JSC.0b013e3182576fa6]
- 13 **Chimera NJ**, Smith CA, Warren M. Injury history, sex, and performance on the functional movement screen and Y balance test.

- J Athl Train* 2015; **50**: 475-485 [PMID: 25761134 DOI: 10.4085/1062-6050-49.6.02]
- 14 **Kraus K**, Schütz E, Taylor WR, Doyscher R. Efficacy of the functional movement screen: a review. *J Strength Cond Res* 2014; **28**: 3571-3584 [PMID: 24918299 DOI: 10.1519/JSC.0000000000000556]
 - 15 **Frohm A**, Heijne A, Kowalski J, Svensson P, Myklebust G. A nine-test screening battery for athletes: a reliability study. *Scand J Med Sci Sports* 2012; **22**: 306-315 [PMID: 21410538 DOI: 10.1111/j.1600-0838.2010.01267.x]
 - 16 **Onate JA**, Dewey T, Kollock RO, Thomas KS, Van Lunen BL, DeMaio M, Ringleb SI. Real-time intersession and interrater reliability of the functional movement screen. *J Strength Cond Res* 2012; **26**: 408-415 [PMID: 22266547 DOI: 10.1519/JSC.0b013e318220e6fa]
 - 17 **Shultz R**, Anderson SC, Matheson GO, Marcello B, Besier T. Test-retest and interrater reliability of the functional movement screen. *J Athl Train* 2013; **48**: 331-336 [PMID: 23675792 DOI: 10.4085/1062-6050-48.2.11]
 - 18 **Butler RJ**, Plisky PJ, Southers C, Scoma C, Kiesel KB. Biomechanical analysis of the different classifications of the Functional Movement Screen deep squat test. *Sports Biomech* 2010; **9**: 270-279 [PMID: 21309301 DOI: 10.1080/14763141.2010.539623]
 - 19 **Hartigan EH**, Lawrence M, Bisson BM, Torgerson E, Knight RC. Relationship of the functional movement screen in-line lunge to power, speed, and balance measures. *Sports Health* 2014; **6**: 197-202 [PMID: 24790688 DOI: 10.1177/1941738114522412]
 - 20 **Kazman JB**, Galecki JM, Lisman P, Deuster PA, O'Connor FG. Factor structure of the functional movement screen in marine officer candidates. *J Strength Cond Res* 2014; **28**: 672-678 [PMID: 23924891 DOI: 10.1519/JSC.0b013e3182a6dd83]
 - 21 **Li Y**, Wang X, Chen X, Dai B. Exploratory factor analysis of the functional movement screen in elite athletes. *J Sports Sci* 2015; **33**: 1166-1172 [PMID: 25465117 DOI: 10.1080/02640414.2014.986505]
 - 22 **Kiesel K**, Plisky PJ, Voight ML. Can Serious Injury in Professional Football be Predicted by a Preseason Functional Movement Screen? *N Am J Sports Phys Ther* 2007; **2**: 147-158 [PMID: 21522210]
 - 23 **Chorba RS**, Chorba DJ, Bouillon LE, Overmyer CA, Landis JA. Use of a functional movement screening tool to determine injury risk in female collegiate athletes. *N Am J Sports Phys Ther* 2010; **5**: 47-54 [PMID: 21589661]
 - 24 **O'Connor FG**, Deuster PA, Davis J, Pappas CG, Knapik JJ. Functional movement screening: predicting injuries in officer candidates. *Med Sci Sports Exerc* 2011; **43**: 2224-2230 [PMID: 21606876 DOI: 10.1249/MSS.0b013e318223522d]
 - 25 **Butler RJ**, Contreras M, Burton LC, Plisky PJ, Goode A, Kiesel K. Modifiable risk factors predict injuries in firefighters during training academies. *Work* 2013; **46**: 11-17 [PMID: 23324700 DOI: 10.3233/WOR-121545]
 - 26 **Warren M**, Smith CA, Chimera NJ. Association of the Functional Movement Screen with injuries in division I athletes. *J Sport Rehabil* 2015; **24**: 163-170 [PMID: 25203695 DOI: 10.1123/jsr.2013-0141]
 - 27 **Garrison M**, Westrick R, Johnson MR, Benenson J. Association between the functional movement screen and injury development in college athletes. *Int J Sports Phys Ther* 2015; **10**: 21-28 [PMID: 25709859]
 - 28 **Hotta T**, Nishiguchi S, Fukutani N, Tashiro Y, Adachi D, Morino S, Shirooka H, Nozaki Y, Hirata H, Yamaguchi M, Aoyama T. Functional Movement Screen for Predicting Running Injuries in 18- to 24-Year-Old Competitive Male Runners. *J Strength Cond Res* 2015; **29**: 2808-2815 [PMID: 25853918 DOI: 10.1519/JSC.0000000000000962]
 - 29 **Knapik JJ**, Cosio-Lima LM, Reynolds KL, Shumway RS. Efficacy of functional movement screening for predicting injuries in coast guard cadets. *J Strength Cond Res* 2015; **29**: 1157-1162 [PMID: 25264669 DOI: 10.1519/JSC.0000000000000704]
 - 30 **McGill S**, Frost D, Lam T, Finlay T, Darby K, Cannon J. Can fitness and movement quality prevent back injury in elite task force police officers? A 5-year longitudinal study. *Ergonomics* 2015; **58**: 1682-1689 [PMID: 25952105 DOI: 10.1080/00140139.2015.1035760]
 - 31 **Beaton DE**, Bombardier C, Katz JN, Wright JG. A taxonomy for responsiveness. *J Clin Epidemiol* 2001; **54**: 1204-1217 [PMID: 11750189]
 - 32 **Bodden JG**, Needham RA, Chockalingam N. The effect of an intervention program on functional movement screen test scores in mixed martial arts athletes. *J Strength Cond Res* 2015; **29**: 219-225 [PMID: 23860293 DOI: 10.1519/JSC.0b013e3182a480bf]
 - 33 **Frost DM**, Beach TA, Callaghan JP, McGill SM. Using the Functional Movement Screen™ to evaluate the effectiveness of training. *J Strength Cond Res* 2012; **26**: 1620-1630 [PMID: 21921825 DOI: 10.1519/JSC.0b013e318234ec59]
 - 34 **Beach TA**, Frost DM, McGill SM, Callaghan JP. Physical fitness improvements and occupational low-back loading - an exercise intervention study with firefighters. *Ergonomics* 2014; **57**: 744-763 [PMID: 24689834 DOI: 10.1080/00140139.2014.897374]
 - 35 **Kiesel K**, Plisky P, Butler R. Functional movement test scores improve following a standardized off-season intervention program in professional football players. *Scand J Med Sci Sports* 2011; **21**: 287-292 [PMID: 20030782 DOI: 10.1111/j.1600-0838.2009.01038.x]
 - 36 **Kiesel KB**, Butler RJ, Plisky PJ. Prediction of injury by limited and asymmetrical fundamental movement patterns in american football players. *J Sport Rehabil* 2014; **23**: 88-94 [PMID: 24225032 DOI: 10.1123/jsr.2012-0130]
 - 37 **Kodesh E**, Shargal E, Kislev-Cohen R, Funk S, Dorfman L, Samuelli G, Hoffman JR, Sharvit N. Examination of the Effectiveness of Predictors for Musculoskeletal Injuries in Female Soldiers. *J Sports Sci Med* 2015; **14**: 515-521 [PMID: 26336337]
 - 38 **Kinzey SJ**, Armstrong CW. The reliability of the star-exursion test in assessing dynamic balance. *J Orthop Sports Phys Ther* 1998; **27**: 356-360 [PMID: 9580895 DOI: 10.2519/jospt.1998.27.5.356]
 - 39 **Hertel J**, Braham RA, Hale SA, Olmsted-Kramer LC. Simplifying the star excursion balance test: analyses of subjects with and without chronic ankle instability. *J Orthop Sports Phys Ther* 2006; **36**: 131-137 [PMID: 16596889 DOI: 10.2519/jospt.2006.36.3.131]
 - 40 **Hertel J**. Sensorimotor deficits with ankle sprains and chronic ankle instability. *Clin Sports Med* 2008; **27**: 353-370, vii [PMID: 18503872 DOI: 10.1016/j.csm.2008.03.006]
 - 41 **Plisky PJ**, Gorman PP, Butler RJ, Kiesel KB, Underwood FB, Elkins B. The reliability of an instrumented device for measuring components of the star excursion balance test. *N Am J Sports Phys Ther* 2009; **4**: 92-99 [PMID: 21509114]
 - 42 **Gribble PA**, Hertel J. Considerations for Normalizing Measures of the Star Excursion Balance Test. *Meas Phys Educ Exerc Sci* 2003; **7**: 89-100 [DOI: 10.1207/S15327841MPEE0702_3]
 - 43 **Plisky PJ**, Rauh MJ, Kaminski TW, Underwood FB. Star Excursion Balance Test as a predictor of lower extremity injury in high school basketball players. *J Orthop Sports Phys Ther* 2006; **36**: 911-919 [PMID: 17193868]
 - 44 **Gribble PA**, Kelly SE, Refshauge KM, Hiller CE. Interrater reliability of the star excursion balance test. *J Athl Train* 2013; **48**: 621-626 [PMID: 24067151 DOI: 10.4085/1062-6050-48.3.03]
 - 45 **Munro AG**, Herrington LC. Between-session reliability of the star excursion balance test. *Phys Ther Sport* 2010; **11**: 128-132 [PMID: 21055706 DOI: 10.1016/j.ptsp.2010.07.002]
 - 46 **Coughlan GF**, Fullam K, Delahunt E, Gissane C, Caulfield BM. A comparison between performance on selected directions of the star excursion balance test and the Y balance test. *J Athl Train* 2012; **47**: 366-371 [PMID: 22889651 DOI: 10.4085/1062-6050-47.4.03]
 - 47 **Fullam K**, Caulfield B, Coughlan GF, Delahunt E. Kinematic analysis of selected reach directions of the Star Excursion Balance Test compared with the Y-Balance Test. *J Sport Rehabil* 2014; **23**: 27-35 [PMID: 23945793 DOI: 10.1123/jsr.2012-0114]
 - 48 **Gribble PA**, Robinson RH, Hertel J, Denegar CR. The effects of gender and fatigue on dynamic postural control. *J Sport Rehabil* 2009; **18**: 240-257 [PMID: 19561367]
 - 49 **Bouillon LE**, Baker JL. Dynamic Balance Differences as Measured

- by the Star Excursion Balance Test Between Adult-aged and Middle-aged Women. *Sports Health* 2011; **3**: 466-469 [PMID: 23016044 DOI: 10.1177/1941738111414127]
- 50 **Butler RJ**, Queen RM, Beckman B, Kiesel KB, Plisky PJ. Comparison of dynamic balance in adolescent male soccer players from rwanda and the United States. *Int J Sports Phys Ther* 2013; **8**: 749-755 [PMID: 24377061]
- 51 **Bressel E**, Yonker JC, Kras J, Heath EM. Comparison of static and dynamic balance in female collegiate soccer, basketball, and gymnastics athletes. *J Athl Train* 2007; **42**: 42-46 [PMID: 17597942]
- 52 **Butler RJ**, Southers C, Gorman PP, Kiesel KB, Plisky PJ. Differences in soccer players' dynamic balance across levels of competition. *J Athl Train* 2012; **47**: 616-620 [PMID: 23182008 DOI: 10.4085/1062-6050-47.5.14]
- 53 **Lehr ME**, Plisky PJ, Butler RJ, Fink ML, Kiesel KB, Underwood FB. Field-expedient screening and injury risk algorithm categories as predictors of noncontact lower extremity injury. *Scand J Med Sci Sports* 2013; **23**: e225-e232 [PMID: 23517071 DOI: 10.1111/sms.12062]
- 54 **Butler RJ**, Lehr ME, Fink ML, Kiesel KB, Plisky PJ. Dynamic balance performance and noncontact lower extremity injury in college football players: an initial study. *Sports Health* 2013; **5**: 417-422 [PMID: 24427412 DOI: 10.1177/1941738113498703]
- 55 **Smith CA**, Chimera NJ, Warren M. Association of y balance test reach asymmetry and injury in division I athletes. *Med Sci Sports Exerc* 2015; **47**: 136-141 [PMID: 24870573 DOI: 10.1249/MSS.0000000000000380]
- 56 **Olivier B**, Stewart AV, Olorunju SA, McKinnon W. Static and dynamic balance ability, lumbo-pelvic movement control and injury incidence in cricket pace bowlers. *J Sci Med Sport* 2015; **18**: 19-25 [PMID: 24268569 DOI: 10.1016/j.jsams.2013.10.245]
- 57 **Basnett CR**, Hanish MJ, Wheeler TJ, Miriovsky DJ, Danielson EL, Barr JB, Grindstaff TL. Ankle dorsiflexion range of motion influences dynamic balance in individuals with chronic ankle instability. *Int J Sports Phys Ther* 2013; **8**: 121-128 [PMID: 23593550]
- 58 **Hoch MC**, Staton GS, McKeon PO. Dorsiflexion range of motion significantly influences dynamic balance. *J Sci Med Sport* 2011; **14**: 90-92 [PMID: 20843744 DOI: 10.1016/j.jsams.2010.08.001]
- 59 **Imai A**, Kaneoka K, Okubo Y, Shiraki H. Comparison of the immediate effect of different types of trunk exercise on the star excursion balance test in male adolescent soccer players. *Int J Sports Phys Ther* 2014; **9**: 428-435 [PMID: 25133071]
- 60 **Imai A**, Kaneoka K, Okubo Y, Shiraki H. Effects of two types of trunk exercises on balance and athletic performance in youth soccer players. *Int J Sports Phys Ther* 2014; **9**: 47-57 [PMID: 24567855]
- 61 **Filipa A**, Byrnes R, Paterno MV, Myer GD, Hewett TE. Neuromuscular training improves performance on the star excursion balance test in young female athletes. *J Orthop Sports Phys Ther* 2010; **40**: 551-558 [PMID: 20710094 DOI: 10.2519/jospt.2010.3325]
- 62 **Garrison JC**, Bothwell J, Cohen K, Conway J. Effects of hip strengthening on early outcomes following anterior cruciate ligament reconstruction. *Int J Sports Phys Ther* 2014; **9**: 157-167 [PMID: 24790777]
- 63 **Ambegaonkar JP**, Mettinger LM, Caswell SV, Burt A, Cortes N. Relationships between core endurance, hip strength, and balance in collegiate female athletes. *Int J Sports Phys Ther* 2014; **9**: 604-616 [PMID: 25328823]
- 64 **Noyes FR**, Barber-Westin SD, Fleckenstein C, Walsh C, West J. The drop-jump screening test: difference in lower limb control by gender and effect of neuromuscular training in female athletes. *Am J Sports Med* 2005; **33**: 197-207 [PMID: 15701605]
- 65 **Hewett TE**, Stroupe AL, Nance TA, Noyes FR. Plyometric training in female athletes. Decreased impact forces and increased hamstring torques. *Am J Sports Med* 1996; **24**: 765-773 [PMID: 8947398]
- 66 **Barber-Westin SD**, Noyes FR, Galloway M. Jump-land characteristics and muscle strength development in young athletes: a gender comparison of 1140 athletes 9 to 17 years of age. *Am J Sports Med* 2006; **34**: 375-384 [PMID: 16282578 DOI: 10.1177/0363546505281242]
- 67 **Ugalde V**, Brockman C, Bailowitz Z, Pollard CD. Single leg squat test and its relationship to dynamic knee valgus and injury risk screening. *PM R* 2015; **7**: 229-235; quiz 235 [PMID: 25111946 DOI: 10.1016/j.pmrj.2014.08.361]
- 68 **Hewett T**, Snyder-Mackler L, Spindler KP. The drop-jump screening test: difference in lower limb control by gender and effect of neuromuscular training in female athletes. *Am J Sports Med* 2007; **35**: 145; author reply 146-147 [PMID: 17197575 DOI: 10.1177/0363546506296609]
- 69 **Noyes FR**, Barber-Westin SD, Smith ST, Campbell T. A training program to improve neuromuscular indices in female high school volleyball players. *J Strength Cond Res* 2011; **25**: 2151-2160 [PMID: 21659890 DOI: 10.1519/JSC.0b013e3181f906ef]
- 70 **Noyes FR**, Barber-Westin SD, Smith ST, Campbell T, Garrison TT. A training program to improve neuromuscular and performance indices in female high school basketball players. *J Strength Cond Res* 2012; **26**: 709-719 [PMID: 22289699 DOI: 10.1519/JSC.0b013e318228194c]
- 71 **Noyes FR**, Barber-Westin SD, Tutalo Smith ST, Campbell T. A training program to improve neuromuscular and performance indices in female high school soccer players. *J Strength Cond Res* 2013; **27**: 340-351 [PMID: 22465985 DOI: 10.1519/JSC.0b013e31825423d9]
- 72 **Barber-Westin SD**, Smith ST, Campbell T, Noyes FR. The drop-jump video screening test: retention of improvement in neuromuscular control in female volleyball players. *J Strength Cond Res* 2010; **24**: 3055-3062 [PMID: 20940643 DOI: 10.1519/JSC.0b013e3181d83516]
- 73 **Padua DA**, Marshall SW, Boling MC, Thigpen CA, Garrett WE, Beutler AI. The Landing Error Scoring System (LESS) Is a valid and reliable clinical assessment tool of jump-landing biomechanics: The JUMP-ACL study. *Am J Sports Med* 2009; **37**: 1996-2002 [PMID: 19726623 DOI: 10.1177/0363546509343200]
- 74 **Padua DA**, Boling MC, Distefano LJ, Onate JA, Beutler AI, Marshall SW. Reliability of the landing error scoring system-real time, a clinical assessment tool of jump-landing biomechanics. *J Sport Rehabil* 2011; **20**: 145-156 [PMID: 21576707]
- 75 **Cortes N**, Onate J. Clinical Assessment of Drop-Jump Landing for Determination of Risk for Knee Injury. *Int J Athl Ther Amp Train* 2013; **18**: 10-13
- 76 **Onate J**, Cortes N, Welch C, Van Lunen BL. Expert versus novice interrater reliability and criterion validity of the landing error scoring system. *J Sport Rehabil* 2010; **19**: 41-56 [PMID: 20231744]
- 77 **Lam KC**, Valovich McLeod TC. The impact of sex and knee injury history on jump-landing patterns in collegiate athletes: a clinical evaluation. *Clin J Sport Med* 2014; **24**: 373-379 [PMID: 24284948 DOI: 10.1097/JSM.0000000000000053]
- 78 **Beutler A**, de la Motte S, Marshall S, Padua D, Boden B. Muscle strength and qualitative jump-landing differences in male and female military cadets: the jump-acl study. *J Sports Sci Med* 2009; **8**: 663-671 [PMID: 21132103]
- 79 **Gokeler A**, Eppinga P, Dijkstra PU, Welling W, Padua DA, Otten E, Benjaminse A. Effect of fatigue on landing performance assessed with the landing error scoring system (less) in patients after ACL reconstruction. A pilot study. *Int J Sports Phys Ther* 2014; **9**: 302-311 [PMID: 24944848]
- 80 **Kuenze CM**, Foot N, Saliba SA, Hart JM. Drop-Landing Performance and Knee-Extension Strength After Anterior Cruciate Ligament Reconstruction. *J Athl Train* 2015; **50**: 596-602 [PMID: 25978101 DOI: 10.4085/1062-6050-50.2.11]
- 81 **Bell DR**, Smith MD, Pennuto AP, Stiffler MR, Olson ME. Jump-landing mechanics after anterior cruciate ligament reconstruction: a landing error scoring system study. *J Athl Train* 2014; **49**: 435-441 [PMID: 24905666 DOI: 10.4085/1062-6050-49.3.21]
- 82 **Owens BD**, Cameron KL, Duffey ML, Vargas D, Duffey MJ, Mountcastle SB, Padua N, Nelson BJ. Military movement training program improves jump-landing mechanics associated with anterior cruciate ligament injury risk. *J Surg Orthop Adv* 2013; **22**: 66-70 [PMID: 23449058]
- 83 **Distefano LJ**, Distefano MJ, Frank BS, Clark MA, Padua DA.

- Comparison of integrated and isolated training on performance measures and neuromuscular control. *J Strength Cond Res* 2013; **27**: 1083-1090 [PMID: 23364296 DOI: 10.1519/JSC.0b013e318280d40b]
- 84 **Padua DA**, DiStefano LJ, Marshall SW, Beutler AI, de la Motte SJ, DiStefano MJ. Retention of movement pattern changes after a lower extremity injury prevention program is affected by program duration. *Am J Sports Med* 2012; **40**: 300-306 [PMID: 22064608 DOI: 10.1177/0363546511425474]
- 85 **Padua DA**, DiStefano LJ, Beutler AI, de la Motte SJ, DiStefano MJ, Marshall SW. The Landing Error Scoring System as a Screening Tool for an Anterior Cruciate Ligament Injury-Prevention Program in Elite-Youth Soccer Athletes. *J Athl Train* 2015; **50**: 589-595 [PMID: 25811846 DOI: 10.4085/1062-6050-50.1.10]
- 86 **Smith HC**, Johnson RJ, Shultz SJ, Tourville T, Holterman LA, Slaughterbeck J, Vacek PM, Beynnon BD. A prospective evaluation of the Landing Error Scoring System (LESS) as a screening tool for anterior cruciate ligament injury risk. *Am J Sports Med* 2012; **40**: 521-526 [PMID: 22116669 DOI: 10.1177/0363546511429776]
- 87 **Myer GD**, Ford KR, Hewett TE. Tuck Jump Assessment for Reducing Anterior Cruciate Ligament Injury Risk. *Athl Ther Today* 2008; **13**: 39-44 [PMID: 19936042]
- 88 **Myer GD**, Brent JL, Ford KR, Hewett TE. Real-time assessment and neuromuscular training feedback techniques to prevent ACL injury in female athletes. *Strength Cond J* 2011; **33**: 21-35 [PMID: 21643474 DOI: 10.1519/SSC.0b013e318213afa8]
- 89 **Myer GD**, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior cruciate ligament reconstruction: criteria-based progression through the return-to-sport phase. *J Orthop Sports Phys Ther* 2006; **36**: 385-402 [PMID: 16776488 DOI: 10.2519/jospt.2006.2222]
- 90 **Herrington L**, Myer GD, Munro A. Intra and inter-tester reliability of the tuck jump assessment. *Phys Ther Sport* 2013; **14**: 152-155 [PMID: 23084318 DOI: 10.1016/j.ptsp.2012.05.005]
- 91 **Dudley LA**, Smith CA, Olson BK, Chimera NJ, Schmitz B, Warren M. Dudley LA, Smith CA, Olson BK, Chimera NJ, Schmitz B, Warren M. Interrater and intrarater reliability of the Tuck Jump Assessment by health professionals of varied educational backgrounds. *J Sports Med* 2013; **2013**: 1-5 [DOI: 10.1155/2013/483503]
- 92 **Hewett TE**, Myer GD, Ford KR, Heidt RS, Colosimo AJ, McLean SG, van den Bogert AJ, Paterno MV, Succop P. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med* 2005; **33**: 492-501 [PMID: 15722287 DOI: 10.1177/0363546504269591]
- 93 **Paterno MV**, Ford KR, Myer GD, Heyl R, Hewett TE. Limb asymmetries in landing and jumping 2 years following anterior cruciate ligament reconstruction. *Clin J Sport Med* 2007; **17**: 258-262 [PMID: 17620778 DOI: 10.1097/JSM.0b013e31804c77ea]
- 94 **Boden BP**, Sheehan FT, Torg JS, Hewett TE. Noncontact anterior cruciate ligament injuries: mechanisms and risk factors. *J Am Acad Orthop Surg* 2010; **18**: 520-527 [PMID: 20810933]
- 95 **Noyes FR**, Barber SD, Mangine RE. Abnormal lower limb symmetry determined by function hop tests after anterior cruciate ligament rupture. *Am J Sports Med* 1991; **19**: 513-518 [PMID: 1962720]

P- Reviewer: Anand A, Chen C, Finestone AS, Franklyn M, Luo XH
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Wu HL



Understanding the pathogenesis of hip fracture in the elderly, osteoporotic theory is not reflected in the outcome of prevention programmes

Enrique Guerado, Rosa M Sandalio, Zaira Caracuel, Enrique Caso

Enrique Guerado, Department of Orthopaedic Surgery and Traumatology, Hospital Costa del Sol, University of Malaga, 29603 Malaga, Marbella, Spain

Rosa M Sandalio, Zaira Caracuel, Enrique Caso, Research Unit, Hospital Costa del Sol, University of Malaga, 29603 Malaga, Marbella, Spain

Author contributions: Guerado E directed the paper, and wrote "The Medical Problem" and "The Social Problem"; Sandalio RM wrote "Genomics"; Caracuel Z wrote "Metabolomics"; Caso E wrote "Transcriptome"; the all authors were involved in editing the manuscript.

Conflict-of-interest statement: The authors declare not conflict of interest. No potential bias in a study's design, interpretation of it results or presentation of its scientific/medical content, including but not limited to commercial, personal, political, intellectual, or religious interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Enrique Guerado, Professor, Chairman, Department of Orthopaedic Surgery and Traumatology, Hospital Costa del Sol, University of Malaga, Autovia A-7. Km 187, 29603 Malaga, Marbella, Spain. eguerado@hcs.es
Telephone: +34-95-1976224

Received: October 28, 2015

Peer-review started: November 3, 2015

First decision: November 30, 2015

Revised: December 19, 2015

Accepted: December 29, 2015

Article in press: January 4, 2016

Published online: April 18, 2016

Abstract

Hip fractures are an acute and worsening public health problem. They mainly affect elderly people, a population group that is highly vulnerable to disease and accidents, and to falls in particular. Although it has been suggested that osteoporosis is the cause of hip fractures, they mainly occur after a fall has been suffered. The underlying causes of a fall are not related to osteoporosis, although pharmaceutical companies have coined the term "osteoporotic fracture" for hip fractures in the elderly. Drug treatments for osteoporosis have not diminished the frequency of these injuries, nor have they prevented the occurrence of a subsequent fracture. Since pharmaceutical interests require osteoporosis to be considered a disease, rather than a normal condition of senescence, they go further by assuming that treatment for osteoporosis is essential, and that this policy will diminish the incidence of hip fractures. On the other hand, the origin and treatment of conditions that may be conducive to provoking falls are very difficult to elucidate. In this paper, we consider some of the medical and social problems that arise in this area, as well as conflicts of interest regarding the aetiopathogenesis and prevention of hip fracture, and propose a new paradigm for the prevention of falls.

Key words: Hip fracture; Osteoporosis; Overtreatment; Social medicine; Political economy; Political actions; Conflict of interest; Genome; Transcriptome; Metabolome

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This paper rejects the role of osteoporosis in the pathogenesis of hip fracture and proposes medically-based political action to support new omics technologies to detect the risk of falls by elderly people, by detracting resources from those currently employed

in the treatment of osteoporosis.

Guerado E, Sandalio RM, Caracuel Z, Caso E. Understanding the pathogenesis of hip fracture in the elderly, osteoporotic theory is not reflected in the outcome of prevention programmes. *World J Orthop* 2016; 7(4): 218-228 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/218.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.218>

INTRODUCTION

In developed countries, hip fracture is a major public health problem. Increased life expectancy, in conjunction with social changes, has made many elderly persons vulnerable to loneliness and to disability. This population group tends to suffer more frequently from hip fracture because they have a higher propensity to falls, as a result of sensorial and neurological deterioration, together with muscular atrophy. Any elderly person, irrespective of concurrent osteoporosis, may suffer a hip fracture because, apart from the unusual case of pathological fracture, a traumatism is a necessary cause^[1]. In other words, in the absence of a fall, hip fracture is very unlikely to occur.

Nevertheless, world-wide programmes to address the question have not been undertaken in accordance with this pathogenic outlook. On the one hand, new and more expensive drugs are continuously being marketed for the treatment of osteoporosis, holding this disease primarily responsible for the occurrence of hip fracture, although such drugs have never been shown to diminish its prevalence or to avoid secondary effects^[2]. On the other hand, financial support for these treatments is becoming even more restricted as national health services are forced to cut budgets. Thus, expensive pharmacologic treatment for osteoporosis adds an extra burden to the cost of providing for the needs of elderly patients. The treatment is purported to reduce the incidence of hip fracture, but the practical outcome is a significant reduction in the options open to the public welfare system, with particular regard to pensions, and in consequence many elderly people lack the means to cope with this situation.

Therefore the problem of hip fracture is twofold: Medical and social. Any approach to this pathology must take into account both aspects, if health policies for hip fracture prevention are to be successful.

THE MEDICAL PROBLEM

Falls are known to be the main cause of hip fracture. However, this pathology is commonly held to be closely related to osteoporosis. The pharmaceuticals industry has coined the term "osteoporotic fracture" for any fracture suffered by an elderly person. Although all elderly people do indeed present osteoporosis, among

other aspects of their health status, they may also be affected by heart disease, stroke or ocular or inner-ear balance problems, any one of which may provoke a fall. However, the fracture is never called an "ophthalmic fracture" or a "labyrinth fracture".

Since osteoporosis alone never provokes a fall, and as a fall is the main antecedent of a hip fracture, there must be some mismatch in the assumption of causality between osteoporosis and hip fracture, *i.e.*, in the pathogenesis of this condition. Osteoporosis only helps to fracture a bone with less energy than non-osteoporotic bone. It has been established that although all elderly people present osteoporosis, only some will suffer a fall, and that less than half of those having a fall will suffer any injury as a result of it^[3]. Moreover of the persons aged 65 years or older who do suffer a fall, over half will experience a repeat of this event within a year^[4]. Although these persons may or may not suffer a hip fracture, pharmaceutical companies cite this circumstance to argue that persons who have had an "osteoporotic fracture" need treatment to prevent the occurrence of a second one. It has been claimed that in order to prevent hip fractures, the supposed bone metabolism disorder that diminishes "bone strength" should be treated. Nevertheless, the available evidence does not show that, as discussed below.

The oral intake of vitamin D, with or without calcium, is the classical treatment for osteoporosis. Nonetheless, low plasma 25-hydroxy vitamin D concentration is associated with high arterial blood pressure and the risk of hypertension^[5], and therefore a constant therapy of vitamin D, either alone or combined with calcium, for the prevention and treatment of osteoporosis, in the absence of explicit risk factors for vitamin D deficiency, appears to be inappropriate^[6,7]. Indeed, this therapy may provoke a significant rise in gastrointestinal symptoms and renal diseases^[6]. Yet despite the dangers, nearly half of all over-50s continue to use these supplements^[8]. The effect of vitamin D on the mortality of the elderly is in fact very odd: Whereas vitamin D3 seems to decrease mortality, vitamin D2, alfacalcidol and calcitriol apparently have no beneficial effects at all^[6], and may even provoke hypercalcaemia; moreover, if vitamin D3 is administered together with calcium supplementation, the risk of nephrolithiasis is increased^[7]. However, the current use of vitamin D by elderly people as a strategy for the prevention of hip fracture could be promoted just for its effects on muscular atrophy. This would reinforce the hypothesis that hip fracture is provoked by a fall, not by osteoporosis.

Mineralisation deficit has also been proposed as a cause of "bone weakness" making elderly persons liable to suffer an "osteoporotic" hip fracture. But according to recent studies, the problem of mineralisation in elderly people is not one of a regular decrease of calcium in the bone, but rather the irregular distribution of its mineralisation. Tissue mineral density is significantly

higher in the periosteal, and decreases from there to the endostium; it diminishes from the distal to the proximal part of the femur neck, and thus varies in a radial fashion. In addition, tissue variations in the axial direction of the femoral neck are responsible for important alterations in bone elasticity. Therefore, this spatial heterogeneity of elastic coefficients of bone tissue has consequences for bone as an organ^[9,10]. In a similar fashion, mineral crystals at the external cortical bone surfaces of the femoral neck of patients with a fractured hip are larger than in a non-fracture control group. Moreover, the mineral content is higher, with cortical porosity values being almost 35% higher than in control groups, while the osteocyte lacunar number density is significantly lower than in controls^[11]. Consequently, the cortical bone of the superolateral femoral neck of hip fracture patients presents distinct signs of fragility at various levels of its structure^[12]. These findings could be very important to understanding the pathogenesis of bone weakness in hip fractures. Hence, merely providing "remineralising" drugs to prevent the occurrence of hip fracture appears too simple a notion. Recent research findings have further reinforced the hypothesis that hypermineralisation and the heterogeneity of mineralisation patterns are at the root of bone fragility^[9-12].

An increased mineral content of bone tissue, in addition to heightened porosity, has also been observed in femur bone obtained from autopsies^[13], with the consequent deleterious effects on bone strength and the risk of fracture.

The calcium-phosphorus ratio does not vary between hypermineralised osteocyte lacunae and bone matrix, according to studies of osteoporotic patients and an osteoarthritic control group. The role of hypermineralised osteocyte lacunae in the biomechanical properties of bone is not totally clear, but investigating the relation between hypermineralisation and femoral neck fracture susceptibility would constitute a very interesting line of research to obtain a better knowledge of the bone stiffness-flexibility relation. Previous studies have found that bone fragility may be greatly increased in the presence of bone tissue heterogeneity in osteons and interstitial tissue^[12], and other researchers have reported that the degree of bone tissue mineralisation is significantly lower in the osteons than in the interstitial tissue both in hip fracture patients and in controls, whereas the presence of osteons and interstitial tissue is significantly greater in hip fracture patients. These data further support the view that bone fragility may be related to a higher degree of tissue mineralisation^[14].

We performed similar studies, but retrieving the bone samples from the base of the femoral neck, as in osteoarthritis the femoral head becomes very dense, and obtaining the samples from this area might provoke a bias, in comparison with samples from osteoporosis patients. We determined microcrystalline salt standards in order to quantify Ca and P, in accordance with the

methods reported in previous publications by our group^[15]. All results were calculated as the weight fraction percentage of Ca and P^[16]. Cancellous bone in hip osteoarthritis was found to be stoichiometrically similar to normal bone; that is to say, it is characterised by a Ca/P molar ratio corresponding to hydroxyapatite. However, the cancellous bone in hip fracture patients had an increased Ca/P ratio, associated with higher concentrations of Ca and P. We believe this further refutes the idea that calcium intake should be increased or drugs administered to "improve mineralisation" in osteoporotic patients and thus prevent hip fracture (unpublished data). The determination of Ca and P fractions in bone mineral density (BMD) in order to enhance fracture risk assessment and thus enable more targeted therapies to be devised has also been recommended^[17].

Other therapies intended to diminish the risk of hip fracture, such as the combination of anabolic agents with bisphosphonates, have had little success. Similarly, the combination of teriparatide and denosumab, although increasing the bone matrix density more than is achieved by either agent alone^[18], not only does not reduce the risk of fracture but may also produce long-term collateral effects. These new therapies, targeted at inhibiting bone resorption and enhancing bone formation, through a better understanding of the signalling network for osteoblast-osteoclast coupling, will allow novel therapeutic targets to be established for osteoporosis treatment but they have nothing to do with decreasing the risk of hip fracture. Denosumab, a monoclonal antibody for the receptor activator of the NF- κ B ligand, a key osteoclast cytokine; odanacatib, a specific inhibitor of the osteoclast protease cathepsin K; and antibodies against the proteins sclerostin and dickkopf-1, two endogenous inhibitors of bone formation, have all achieved promising results in the treatment of osteoporosis^[19].

Therefore, if osteoporosis were the cause of hip fracture, then by treating osteoporosis many fractures could be prevented. However, as the real causal framework is different, the following questions (and answers) arise. What actually provokes a fracture? In many cases, a fall and what provokes a fall? In many cases, a sensory deficit and which sensory deficits are capable of provoking a fall? Apparently, ophthalmic and/or auditory disorders, brain disease or reduced mobility. In consequence, taking action to prevent falls caused by these circumstances will reduce the prevalence of hip fracture. Unfortunately, comparison between races (Caucasian vs Asian, and particularly to black race) is very difficult as social situation are different.

THE SOCIAL PROBLEM

Funding

Undoubtedly, if pharmacological treatment for osteoporosis were the solution for "osteoporotic" hip fractures, financial support for this purpose would be

needed. Funding would have to be obtained either directly, from the patient, or indirectly, *via* a public welfare system. Since the end of World War 2, European welfare systems, based on principles of solidarity, have been the linchpins of funding for disease prevention and treatment programmes. However, following the onset of the economic crisis in 2007, governments have declared that such systems are no longer sustainable. National health service budgets have been slashed throughout Europe^[20], but in many countries pharmaceutical expenses are either still rising or are falling at a slower rate than other items in health system budgets, thus forming a recurrent financial problem that presents a major challenge to society.

In Europe, national health services spent typically accounts for 6%-12% of Gross Domestic Product (GDP), but elsewhere the situation may be very different. Thus, in the United States, where a more market-oriented system exists, health spending represents nearly 18% of GDP. Nevertheless, a large sector of the population remains without access to a good quality health service. Private medical insurance can be crippling expensive, and many are forced to do without in order to meet day-to-day living costs. The Health Alliance International of the Washington University School of Public Health has reported that for this reason millions of persons in the first world are condemned to suffer avoidable disease and early death^[21].

The austerity policies currently being applied throughout Europe slow economic growth and hamper the repayment of external debt^[22-24]. Paul Krugman, the Nobel Prize-winning economist, has advocated raising government budgets for public welfare policies, including health programmes^[25,26]. Similar conclusions were drawn by Greek authors in a recent paper published in the *Lancet*^[27].

National policies to prevent hip fracture need generous budgets, but since spending cannot rise indefinitely, national budgets for healthcare policies must be focused on efficiency and effectiveness. Thus, current spending on ineffective medicaments should be readdressed toward effective medical actions, and as the medical treatment of osteoporosis does not reduce the prevalence of hip fracture^[2,8,28,29], the national health services budgets for such treatments should be reassigned toward social support, particularly fall prevention. The question remains: Will national governments do so?

The power of pharmaceutical companies

There is much current debate concerning the real need for medicaments. An increasing number of doctors are convinced that a significant proportion of the drugs currently prescribed are ineffectual if not actually harmful^[28-44]. Obviously, many drugs are necessary and valuable, but pharmaceutical and medical device companies often trial their products among the most favourable population and comparison groups in order

to obtain the most positive outcomes for their interests. Company staff controls the data and perform the analyses in-house, while academic researchers are often paid to be listed among the authors when in fact they have contributed little and cannot vouch for the data presented; although difficultly, current rules, and regulations try to avoid that. Many "opinion leaders" work for pharmaceutical companies as advisers, and most doctors on the committees of scientific societies have links to companies that are an important source of funds to these societies^[28]. In many cases, too, trials with negative results are suppressed and remain unpublished^[29-31]. In the nineteenth century, Quetelet^[30] observed, "society prepares the crime and the guilty person is only the instrument by which it is executed", and this proposition is still applicable today.

Drug companies are very powerful and have often been accused of making illicit payments to individuals or institutions to further their ends. In addition, many have been convicted of marketing harmful - often fatal - drugs, of committing fraud, of manipulating prices and of concealing evidence^[31]. The fines levied against drug companies for these offences are insignificant in comparison to the enormous profits obtained, and are often regarded as merely the cost of doing business^[31]. In 2012, a major United States pharmaceutical company agreed to pay a fine of \$60.2 million in order to forestall an investigation into the corruption of foreign doctors, hospital managers and pharmaceutical controllers in Europe and Asia^[32].

Both in the United States and elsewhere, the large pharmaceutical concerns head the ranking of the most unlawful companies^[31,33]. In the United States, the drug market is regulated by politicians, who have come to be a prime target for industry lobbying^[31]. At one point, indeed, the United States Secretary of Defense was at the same time the Chief Executive Officer of an important pharmaceutical company, while the budget director of the White House later became Vice-President of a top drug company, and the President himself was a member of the board of this company before coming into power^[28].

The same conflict of interest issue has occurred in the United Kingdom. Thus, in 2005 the House of Commons Health Committee highlighted the enormous and uncontrolled power of the pharmaceutical industry, and accused it of exerting pressure on doctors, Non-governmental organizations, patients' associations, journalists and politicians^[34-37]. Nevertheless, after receiving this report, the British Government did nothing to change the situation - an outcome influenced by the fact that the pharmaceutical industry, after tourism and finance, is the most profitable business activity in the country^[31,35].

Several books have analysed this problem in detail, including a recent very well documented one by the director of the Nordic Cochrane Centre^[31], two by past editors of the *New England Journal of Medicine*^[28,38] and

one by an editor of the *British Medical Journal*^[39]. Other publications have reported on abuses in specific medical fields^[40-42] and on the scourge of overdiagnosis^[29,43,44].

Are osteoporosis patients victims of this conflict of interests?

The treatment of osteoporosis is also affected by the above-described conflict of interests. In 2005, a major drug company agreed to pay \$36 million to settle criminal and civil charges related to the illegal marketing of raloxifene, a drug used in the treatment of osteoporosis. The company had claimed this medication prevented breast cancer and cardiovascular diseases, but failed to reveal that it also increased the risk of ovary cancer^[31].

The problem in this context begins with the very definition of osteoporosis. The pharmaceutical industry, among others, sponsors the definition of diseases^[45,46]. Although osteoporosis is defined as a metabolic disorder characterised by decreased bone mass and deteriorated bone structure, resulting in an increased susceptibility to fractures^[47], osteoporosis - the visual image of osteopaenia - is actually a normal skeletal situation among elderly people. The World Health Organization (WHO) definition of osteoporosis is based on bone density data presented by young women^[48], which has nothing to do with the situation of elderly persons, among whom bone deterioration is just a part of body decline in general. No objective reason was presented by the WHO group on osteoporosis when it was decided that anyone with a BMD that lies 2.5 standard deviations or more below the average value for young healthy women would be considered as having osteoporosis^[48]. However, so far, no an alternative standard has been published.

On the basis of the WHO definition, densitometry is considered by patients' associations to be the gold standard for the diagnosis of osteoporosis. However, according to technological evaluation agencies, the truth is quite the opposite^[31]. Both the defining body and many patients' associations are funded by pharmaceutical companies^[31], which have an evident interest in ensuring that all persons presenting osteoporosis, under the WHO densitometry definition, should receive pharmaceutical treatment^[48]. It has been shown that all post-menopausal women will present osteoporosis. In consequence, according to the drug companies' approach, from a given age, at least half of the entire population should be pharmacologically treated for this disease. In fact, the evidence base has been systematically distorted, and evidence-based medicine and guidelines have been hijacked by pharmaceutical companies^[49,50].

Health technology agencies have published data obtained from five independent evaluations of the predictive performance of bone density measurements. Depending on the threshold values used and the assumed lifetime incidence of hip fracture, these studies have reported predictive values for positive

results in BMD tests ranging from 8% to 36%^[51]. Similarly, recent systematic reviews have concluded that there is insufficient evidence to inform the choice of which bone turnover marker to use in routine clinical practice to monitor the response to osteoporosis treatment. Consequently, the research priority should be to identify the most promising treatment-test combinations for evaluation in subsequent, methodologically sound, randomised controlled trials (RCTs), in order to determine whether or not bone turnover marker monitoring actually improves treatment management decisions, and ultimately impacts on patient outcomes in terms of reduced incidence of fracture. Given the large number of potential patient population-treatment test combinations, the most promising combinations would initially need to be identified in order to ensure that the RCTs focus on evaluating those strategies^[52]. Such projects should also focus on the multifactorial etiology (co-morbidity, type and circumstances of trauma, polypharmacy, previous fractures, hereditary, menopause, etc.) of broken bones. International registries are a major step forward to this approach.

BMD studies do not predict hip fracture and long-term pharmacological treatment for osteoporosis does not reduce the incidence of hip fracture cases^[53]. Furthermore since the new drug-induced bone formed has not a normal structure, iatrogenic fractures can appear. The majority of women of menopausal age are at low risk of "osteoporotic" fracture in the short-medium term. If BMD testing leads to unnecessary treatment and anxiety (typical effects of disease mongering), it may do more harm than good^[45].

Moynihan *et al*^[45] suggest that preventive medicine is threatening the viability of publicly funded healthcare systems, and that osteoporosis has been effectively sponsored by the pharmaceutical industry. Too many people who fall and develop a fracture are considered for treatment of osteoporosis^[45]. Conversely, systematic reviews of randomised trials have shown that the decline in BMD is attenuated with exercise^[54,55], and one such review found that some forms of supervised exercise increase muscle mass and reduce the incidence of falls^[56]. Observational studies have shown there is a protective association between regular exercise and hip fracture^[57].

The field of osteoporosis is an obscure one, particularly when conflicts of interest arise in addressing the relationship between osteoporosis and hip fracture. There are three main reasons why a patient with osteoporosis or any disease may experience symptomatic improvement: Medicament effect, placebo effect and the natural course of the disease. Most published reports of patient improvement are strongly affected by bias^[31]. In the field of orthopaedics, unfounded research claims have been made by companies manufacturing joint implants^[58,59]. Apart from medical researchers and physicians, scientific journals also seem to have been affected by dishonest reporting^[60]. Osteoporosis associations reject comments on their funding^[61], but the

fact is that while some osteoporosis associations receive funding from government agencies, lists of commercial sponsors also appear on their websites^[28,31,45].

A PROPOSED NEW PARADIGM FOR THE AETIOPATHOGENESIS OF HIP FRACTURE IN THE ELDERLY: THE BASIS OF PREVENTION

Since hip fracture is usually caused by a fall, by identifying the population with a propensity to suffer a fall, *i.e.*, those with a sensory or cognitive problem aggravating the risk of a fall, and then providing proper treatment for such problems, both falls and hip fractures could be prevented.

Each year, approximately 30% of non-institutionalised persons aged over 65 years suffer a fall. Group and home-based exercise programmes and home safety interventions can reduce the risk and hence the rate of falls^[54,55]. Multifactorial assessment and public health intervention programmes, on the other hand, reduce the rate of falls but not the risk of falling; certain specific forms of exercise, such as Tai Chi, also reduce the risk of falling. Vitamin D supplementation does not appear to reduce the risk or rate of falls but may be effective in people who have low levels of vitamin D before treatment^[56].

Hip protectors probably reduce the risk of hip fractures when provided to older people in nursing care or residential care settings, without increasing the frequency of falls. However, since they are very uncomfortable, patients keep them in the wardrobe. They also may slightly increase the risk of pelvic fractures. Poor acceptance and adherence by older people offered hip protectors is a barrier to their use^[62].

Together with these physical actions to prevent falls, some basic lines of scientific research must be undertaken to establish a new paradigm. In this respect, genetic research has been employed to address the question of osteoporosis. It has been reported that two gene variants of key biological proteins can increase the risk of osteoporosis and osteoporotic fracture. The combined effect of these risk alleles on fractures is similar to that of most well-replicated environmental risk factors, and they are present in more than one in five white people, suggesting a potential role in screening^[63]. Although the authors of this paper studied the risk of osteoporosis they did not consider the risk of fracture or of falls. Another study, in an *in vivo* analysis of zebrafish, examined the bone regulatory properties of plastin 3 (PLS3), a protein involved in the formation of filamentous actin (F-actin) bundles, and found it to be related to osteogenesis imperfecta type I, with a rare variant (rs140121121) in PLS3. The association of this variant with the risk of fracture among elderly heterozygous women indicates that genetic variation in PLS3 is a novel aetiological factor that is involved in common, multi-factorial osteoporosis^[64]. The question

then arises: How many elderly persons present this complex mechanism, which, according to theory, can account for the risk of hip fracture?

One thing is to alleviate osteoporosis but quite another to imagine that, even if this were achieved, it would prevent or reduce the incidence of hip fracture. New research into "omics" is enhancing our understanding of the pathogenesis of osteoporosis, but this does not mean that a new paradigm for the aetiopathogenesis of hip fractures is being created. Again, in accordance with the real causality framework that has been established, research should be focused, not on osteoporosis, but on preventing falls by vulnerable persons. New findings in the fields of the human genome, transcriptome and metabolomics, if appropriately addressed, would reveal the susceptibility of elderly people to falls and thus open the way to preventing many hip fractures.

Genome

The completion of the Human Genome Project^[65], followed by the development of a more manageable understanding of the human genome in the Hap Map Project^[66] and the launch of Genome-Wide Association Studies (GWAS)^[67], marked a great accomplishment and initiated a burst in scientific discovery of the genetic underpinnings of common diseases. Therefore it is expected that our knowledge of the factors provoking falls will also benefit from genome studies.

GWAS have located most of the very common gene variants in the human genome and have identified over 500 independent strong single nucleotide polymorphism associations. The 1000 Genomes Project^[68] and the UK10K Project^[69] are population-level sequencing projects that have led to an explosive growth of individual whole genome sequencing (WGS) data.

In the post-genomic era, next-generation sequencing (NGS) technologies have become more accessible in terms of cost, analytic validity and rapidity. Whole-exome sequencing (WES) using NGS has the capacity to determine in a single assay an individual's exomic variation profile, limited to about 85% of the protein coding sequence of an individual, composed of some 20000 genes, 180000 exons, and constituting approximately 1% of the whole genome. A sensitivity of 98.3% for detecting previously identified mutations, as well as benign variants, has been reported by WES^[70]. Furthermore, WES allows the phenotype expansion and identification of new candidate disease genes that would have been impossible to diagnose by other targeted testing methods^[70]. Proof-of-concept examples of the identification of rare, disease-causing variants are now available for WGS and WES strategies^[71-73]. A major indication for their use is the molecular diagnosis of patients with suspected genetic disorders or that of patients with known genetic disorders with substantial genetic heterogeneity involving significant gene complexity. Particular limitations in WES are the gaps in coverage of the exome, the difficulty of finding

the causal mutation among the enormous background of individual variability in a small number of samples, and the difficulty interpreting variants. It is in this field of work where new bioinformatic tools are currently of great assistance to researchers. A large database would be of great benefit in producing a profile of elderly people predisposed to suffer falls.

Transcriptome

The transcriptome is the complete set of transcripts in a cell, and their quantity, for a specific developmental stage or physiological condition. Understanding the transcriptome is essential for interpreting the functional elements of the genome and revealing the molecular constituents of cells and tissues, and also for understanding development and disease. The key aims of transcriptomics are: (1) to catalogue all species of transcript, including mRNAs, non-coding RNAs and small RNAs; (2) to determine the transcriptional structure of genes, in terms of their start sites, 5' and 3' ends, splicing patterns and other post-transcriptional modifications; and (3) to quantify the changing expression levels of each transcript during development and under different conditions^[74]. The human transcriptome is comprised of over 80000 protein-encoding transcripts and the estimated number of proteins synthesised from these transcripts is in the range of 250000 to 1000000. These transcripts and proteins are encoded by fewer than 20000 genes, suggesting a wide regulation of transcription, at the post-transcriptional and translational levels. RNA sequencing (RNA-seq) technologies have increased our understanding of the mechanisms that give rise to alternative transcripts and translations^[75]. Next-generation sequencing technologies are evolving rapidly and it is likely that RNA-seq will become routine for many laboratories in coming years. Sequencers are becoming smaller and more personal and are beginning to equip individual departments and laboratories. Library preparation protocols are also becoming shorter and more efficient. Single molecule sequencing will afford insights into the precise orientation of transcription. Advances in methods to acquire sequences are likely to be accompanied by equally rapid advances in computation and data analysis^[76].

The study of transcriptome allows us a deeper understanding of the pathogenesis of various diseases and makes it possible to select biomarkers to facilitate the early detection and therapeutic monitoring of these diseases. Recently published studies have compared healthy bone tissue with that of patients diagnosed with osteosarcoma (OS). Differences in the expression of certain genes were found between these experimental groups. These genes appear to be involved in the development of OS or other cancers, and could be used as biomarkers or as new drug targets^[77]. Other studies have shown how multiple transcription factors and multiple signal transduction pathways are coordinated and temporally regulated during endochondral bone formation. Modelling these pathways and the intera-

ctions of groups of strain-specific genes will allow us to infer the interactions between transcription factors and signal transduction pathways that coordinate the training of vascular and skeletal tissues^[78].

The study of bone transcriptome can enhance our understanding of the pathogenesis of hip fracture, enabling us to select biomarkers and thus facilitate early detection of elderly persons' susceptibility to falling. Nevertheless costs of these projects, and, if possible, therapy for these patients are unknown.

Metabolomics

Metabolomics is an emerging multidisciplinary science that requires cooperation between chemists, biologists and computer scientists. The metabolome refers to the complete inventory of small molecules, non-protein compounds, such as metabolic intermediates (ATP, fatty acids, glucose, cholesterol, hormones and other signalling molecules), and secondary metabolites found in a biological sample^[79,80].

The metabolome changes continuously, depending on the activation and interaction of the various metabolic pathways within the cell. It also reflects the phenotype that can be used to interfere with gene function. Although genomics and proteomics can provide important information on the expected function, metabolomics provides an immediate snapshot of all biological functions that reflect current events at an exact moment^[81,82]. By measuring the population of biomarkers (metabolites), it may be possible to distinguish the profiles or signatures of healthy individuals from those of persons with specific diseases^[83]. Moreover, metabolomics may provide evidence of a metabolic disorder or injury with a high degree of precision and at less cost than by means of genomics, transcriptomics or proteomics. Therefore, it is a very suitable technique for generalised research in life sciences^[84,85]. In the last decade of development of spectrometry, metabolic profiling using high-resolution magic-angle-spinning nuclear magnetic resonance (HR-MAS NMR) has made it possible to analyse intact tissue.

This technique has been applied to the study of specific tissue toxicity, to characterise the composition and structure of tissues, and to analyse human samples (such as biopsies, cells or tumours)^[86,87]. In recent years, the number of papers published in this field has grown appreciably, and many of these describe the characterisation of the metabolic profile of different types of human tumours, including brain tumours^[88,89], breast cancer^[90-92], colorectal cancer^[93] and prostate cancer^[94,95]. The fact that no sample processing takes place provides the added advantage that the tissue can be recovered and analysed histologically a posteriori, thus providing the possibility of establishing direct correlations between the metabolic profiles and the histological^[96] or even genomic results^[97].

CONCLUSION

Precision medicine (PM) has the potential to produce

a fundamental change in how health care is practiced, but it does require health care personnel to understand the complexities present in this field. An important component of PM is the use of an individual's genomic information to offer targeted treatment, tailored to the individual. Whether or not the "omic" technologies eventually provide a practical contribution to our understanding of causality, offering significant advances in the real aetiopathogenesis of hip fracture, in any case, they will not appear to be subject to any conflict of interest, although new industries for "omic" technologies are emerging. If this advance comes to pass, will over-diagnosis cease to be a problem caused by scientific misjudgement or by conflicts of interest^[98-100]. The respond will be in the future.

REFERENCES

- Hernlund E, Svedbom A, Ivergård M, Compston J, Cooper C, Stenmark J, McCloskey EV, Jönsson B, Kanis JA. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos* 2013; **8**: 136 [PMID: 24113837 DOI: 10.1007/s11657-013-0136-1]
- Guerado E, Cruz E, Cano JR, Crespo PV, Alaminos M, Sánchez-Quevedo MC, Campos A. Mineralization: Effects on Hip Fractures. *Injury* 2015; **47** Suppl 1: S21-24 [PMID: 26768284 DOI: 10.1016/S0020-1383(16)30005-5]
- To KG, Meuleners L, Bulsara M, Fraser ML, Duong DV, Do DV, Huynh VA, Phi TD, Tran HH, Nguyen ND. A longitudinal cohort study of the impact of first- and both-eye cataract surgery on falls and other injuries in Vietnam. *Clin Interv Aging* 2014; **9**: 743-751 [PMID: 24812501 DOI: 10.2147/CIA.S61224]
- To KG, Meuleners LB, Fraser ML, Do DV, Duong DV, Huynh VA, To QG, Phi TD, Tran HH, Nguyen ND. Prevalence and visual risk factors for falls in bilateral cataract patients in Ho Chi Minh City, Vietnam. *Ophthalmic Epidemiol* 2014; **21**: 79-85 [PMID: 24568591 DOI: 10.3109/09286586.2014.885058]
- Vimaleswaran KS, Cavadino A, Berry DJ, Jorde R, Dieffenbach AK, Lu C, Alves AC, Heerspink HJ, Tikkanen E, Eriksson J, Wong A, Mangino M, Jablonski KA, Nolte IM, Houston DK, Ahluwalia TS, van der Most PJ, Pasko D, Zgaga L, Thiering E, Vitart V, Fraser RM, Huffman JE, de Boer RA, Schöttker B, Saum KU, McCarthy MI, Dupuis J, Herzig KH, Sebert S, Pouta A, Laitinen J, Kleber ME, Navis G, Lorentzon M, Jameson K, Arden N, Cooper JA, Acharya J, Hardy R, Raitakari O, Ripatti S, Billings LK, Lahti J, Osmond C, Penninx BW, Rejnmark L, Lohman KK, Paternoster L, Stolk RP, Hernandez DG, Byberg L, Hagström E, Melhus H, Ingelsson E, Mellström D, Ljunggren O, Tzoulaki I, McLachlan S, Theodoratou E, Tiesler CM, Jula A, Navarro P, Wright AF, Polasek O, Wilson JF, Rudan I, Salomaa V, Heinrich J, Campbell H, Price JF, Karlsson M, Lind L, Michaëlsson K, Bandinelli S, Frayling TM, Hartman CA, Sørensen TI, Kritchevsky SB, Langdahl BL, Eriksson JG, Florez JC, Spector TD, Lehtimäki T, Kuh D, Humphries SE, Cooper C, Ohlsson C, März W, de Borst MH, Kumari M, Kivimäki M, Wang TJ, Power C, Brenner H, Grimnes G, van der Harst P, Snieder H, Hingorani AD, Pilz S, Whittaker JC, Järvelin MR, Hyppönen E. Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study. *Lancet Diabetes Endocrinol* 2014; **2**: 719-729 [PMID: 24974252 DOI: 10.1016/S2213-8587(14)70113-5]
- Avenell A, Mak JC, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database Syst Rev* 2014; **4**: CD000227 [PMID: 24729336 DOI: 10.1002/14651858.CD000227.pub4]
- Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, Bjelakovic M, Gluud C. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev* 2014; **1**: CD007470 [PMID: 24414552 DOI: 10.1002/14651858.CD007470.pub3]
- Reid IR, Bolland MJ, Grey A. Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. *Lancet* 2014; **383**: 146-155 [PMID: 24119980 DOI: 10.1016/S0140-6736(13)61647-5]
- Sansalone V, Bousson V, Naili S, Bergot C, Peyrin F, Laredo JD, Haïat G. Anatomical distribution of the degree of mineralization of bone tissue in human femoral neck: impact on biomechanical properties. *Bone* 2012; **50**: 876-884 [PMID: 22245631 DOI: 10.1016/j.bone.2011.12.020]
- Sansalone V, Bousson V, Naili S, Bergot C, Peyrin F, Laredo JD, Haïat G. Numerical assessment of the effects of the axial variations of porosity and mineralisation on the elastic properties in the human femoral neck. *Comput Methods Biomech Biomed Engin* 2013; **16** Suppl 1: 308-309 [PMID: 23923953 DOI: 10.1080/10255842.2013.815920]
- Milovanovic P, Rakocevic Z, Djonc D, Zivkovic V, Hahn M, Nikolic S, Amling M, Busse B, Djuric M. Nano-structural, compositional and micro-architectural signs of cortical bone fragility at the superolateral femoral neck in elderly hip fracture patients vs. healthy aged controls. *Exp Gerontol* 2014; **55**: 19-28 [PMID: 24614625 DOI: 10.1016/j.exger.2014.03.001]
- Bousson V, Bergot C, Wu Y, Jolivet E, Zhou LQ, Laredo JD. Greater tissue mineralization heterogeneity in femoral neck cortex from hip-fractured females than controls. A microradiographic study. *Bone* 2011; **48**: 1252-1259 [PMID: 21397739 DOI: 10.1016/j.bone.2011.03.673]
- Carpentier VT, Wong J, Yeap Y, Gan C, Sutton-Smith P, Badiei A, Fazzalari NL, Kuliwaba JS. Increased proportion of hypermineralized osteocyte lacunae in osteoporotic and osteoarthritic human trabecular bone: implications for bone remodeling. *Bone* 2012; **50**: 688-694 [PMID: 22173055 DOI: 10.1016/j.bone.2011.11.021]
- Wu Y, Bergot C, Jolivet E, Zhou LQ, Laredo JD, Bousson V. Cortical bone mineralization differences between hip-fractured females and controls. A microradiographic study. *Bone* 2009; **45**: 207-212 [PMID: 19379848 DOI: 10.1016/j.bone.2009.04.202]
- López-Escámez JA, Crespo PV, Cañizares FJ, Campos A. Standards for quantification of elements in the otolithic membrane by electron probe X-ray microanalysis: calibration curves and electron beam sensitivity. *J Microsc* 1993; **171**: 215-222 [PMID: 8246271]
- Sánchez-Quevedo MC, Nieto-Albano OH, García JM, Gómez de Ferraris ME, Campos A. Electron probe microanalysis of permanent human enamel and dentine. A methodological and quantitative study. *Histol Histopathol* 1998; **13**: 109-113 [PMID: 9476640]
- Zoehrer R, Perilli E, Kuliwaba JS, Shapter JG, Fazzalari NL, Voelcker NH. Human bone material characterization: integrated imaging surface investigation of male fragility fractures. *Osteoporos Int* 2012; **23**: 1297-1309 [PMID: 21695535 DOI: 10.1007/s00198-011-1688-9]
- Tsai JN, Uihlein AV, Lee H, Kumbhani R, Siwila-Sackman E, McKay EA, Burnett-Bowie SA, Neer RM, Leder BZ. Teriparatide and denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomised trial. *Lancet* 2013; **382**: 50-56 [PMID: 23683600 DOI: 10.1016/S0140-6736(13)60856-9]
- Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. *Lancet* 2011; **377**: 1276-1287 [PMID: 21450337 DOI: 10.1016/S0140-6736(10)62349-5]
- Tamaki R. OECD Economic Outlook. Developments in individual OECD countries. *OECD Publishing* 2014; **1**: 182 [DOI: 10.1787/eco_outlook-v2014-1-en]
- Fort M, Mercer MA, Gish O. *Sickness and wealth. The corporate Assault on Global Health.* Boston: South End Press, 2004: 105-158
- Shrinking again. Italy slips back into recession. *The Economist.* [updated 2014 Aug 9]. Available from: URL: <http://www.economist>.

- com/news/europe/21611156-italy-slips-back-recession-shrinking-again
- 23 Austerity bites. *The Economist*. [updated 2012 Apr 25]. Available from: URL: <http://www.economist.com/blogs/freeexchange/2012/04/fiscal-policy>
 - 24 Austerity in theory and in practice. *The Economist*. [updated 2012 Aug 17]. Available from: URL: <http://www.economist.com/blogs/freeexchange/2012/08/fiscal-policy>
 - 25 **Krugman P.** Acabad ya con esta crisis. Barcelona: Crítica SL, 2012
 - 26 **Krugman P.** The Deflation Caucus. *The New York Times*. [updated 2014 Sept 4]. Available from: URL: http://www.nytimes.com/2014/09/05/opinion/paul-krugman-the-deflation-caucus.html?_r=0
 - 27 **Kentikelenis A,** Karanikolos M, Papanicolas I, Basu S, McKee M, Stuckler D. Health effects of financial crisis: omens of a Greek tragedy. *Lancet* 2011; **378**: 1457-1458 [PMID: 21988763 DOI: 10.1016/S0140-6736(11)61556-0]
 - 28 **Angell M.** *The Truth About the Drug Companies*. Random House Trade Paperback Edition. New York, 2004
 - 29 **Dickinson JA.** We cannot market the unsaleable. *Can Fam Physician* 2007; **53**: 1149-1150
 - 30 **Quetelet A.** Adolphe Quetelet's Research on the Propensity for Crime at Different Ages. Anderson Publ. Co. 1984. Cincinnati. Available from: URL: <http://www.ncjrs.gov/App/Publications/abstract.aspx?ID=94009>
 - 31 **Gotzsche PC.** Deadly medicines and organised crime. How big pharma has corrupted healthcare. London: Radcliffe Publishing, 2013: 1-322
 - 32 **Rockoff JD,** Matthews CM. Pfizer settles Federal Bribery Investigation. *Wall Street Journal*. [updated 2012 Aug 7]. Available from: URL: <http://www.wsj.com/articles/SB10000872396390444246904577575110723150588>
 - 33 **Clinard MB,** Yeager PC. *Corporate Crime*. New Brunswick: Transaction Publishers, 2006: 55-58
 - 34 **House of Commons Health Committee.** The Influence of the Pharmaceutical Industry. Fourth Report of the Session. [updated 2005 Mar 22]. Available from: URL: <http://www.lindalliance.org/pdfs/HofCHealthCommittee.pdf>
 - 35 **Collier J.** Big pharma and the UK Government. *Lancet* 2006; **367**: 97-98 [PMID: 16413862]
 - 36 **Ferner RE.** The influence of big pharma. *BMJ* 2005; **330**: 855-856 [PMID: 15831847 DOI: 10.1136/bmj.330.7496.855]
 - 37 **Smith R.** Curbing the influence of the drug industry: a British view. *PLoS Med* 2005; **2**: e241 [PMID: 16076242 DOI: 10.1371/journal.pmed.0020241]
 - 38 **Kassirer JP.** *On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health*. New York: Oxford University Press, 2005: 1-272
 - 39 **Smith R.** The trouble with medical journals. *J R Soc Med* 2006; **99**: 115-119 [PMID: 16508048 DOI: 10.1258/jrsm.99.3.115]
 - 40 **Mukherjee S.** *The emperor of all maladies. A biography of cancer*. New York: Scribner, 2010: 1-571
 - 41 **Brawley OW,** Goldberg P. *How we do harm. A doctor breaks ranks about being sick in America*. New York: St Martin's Press, 2012: 1-303
 - 42 **Frances A.** *Saving normal: an insider's revolt against out-of-control psychiatric diagnosis, DSM-5, Big Pharma, and the medicalization of ordinary life*. New York: HarperCollins, 2013: 1-336
 - 43 **Welsh HG,** Schwartz LM, Woloshin S. *Overdiagnosed: making people sick in the pursuit of health*. Boston: Beacon Press, 2011: 1-248
 - 44 **Morgan DJ,** Wright SM, Dhruva S. Update on medical overuse. *JAMA Intern Med* 2015; **175**: 120-124 [PMID: 25365707 DOI: 10.1001/jamainternmed.2014.5444]
 - 45 **Moynihhan R,** Cassels A. *Selling sickness: how the world's biggest pharmaceutical companies are turning us all into patients*. New York, NY: Nation Books, 2005: 1-256
 - 46 **Tiner R.** The pharmaceutical industry and disease mongering. The industry works to develop drugs, not diseases. *BMJ* 2002; **325**: 216; author reply 216 [PMID: 12142315]
 - 47 **Pietschmann P,** Rauner M, Sipos W, Kerschman-Schindl K. Osteoporosis: an age-related and gender-specific disease—a mini-review. *Gerontology* 2009; **55**: 3-12 [PMID: 18948685 DOI: 10.1159/000166209]
 - 48 Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. *World Health Organ Tech Rep Ser* 1994; **843**: 1-129 [PMID: 7941614]
 - 49 **Spencer D.** Evidence based medicine is broken. *BMJ* 2014; **348**: g22
 - 50 **Upshur RE,** Tracy CS. Is evidence-based medicine overrated in family medicine?: Yes. *Can Fam Physician* 2013; **59**: 1160-1161 [PMID: 24235185]
 - 51 **Green CJ,** Bassett K, Foerster V, Kazanjian A. Bone mineral density testing: does the evidence support its selective use in well women? Vancouver. BC: British Columbia Office of Health Technology Assessment. [updated 2002 Feb 10]. Available from: URL: <http://www.chspr.ubc.ca/bcohta/pdf/bmd.pdf>
 - 52 **Burch J,** Rice S, Yang H, Neilson A, Stirk L, Francis R, Holloway P, Selby P, Craig D. Systematic review of the use of bone turnover markers for monitoring the response to osteoporosis treatment: the secondary prevention of fractures, and primary prevention of fractures in high-risk groups. *Health Technol Assess* 2014; **18**: 1-180 [PMID: 24534414 DOI: 10.3310/hta18110]
 - 53 **Abrahamsen B,** Eiken P, Eastell R. Cumulative alendronate dose and the long-term absolute risk of subtrochanteric and diaphyseal femur fractures: a register-based national cohort analysis. *J Clin Endocrinol Metab* 2010; **95**: 5258-5265 [PMID: 20843943 DOI: 10.1210/jc.2010-1571]
 - 54 **Wolff I,** van Croonenborg JJ, Kemper HC, Kostense PJ, Twisk JW. The effect of exercise training programs on bone mass: a meta-analysis of published controlled trials in pre- and postmenopausal women. *Osteoporos Int* 1999; **9**: 1-12 [PMID: 10367023]
 - 55 **Wallace BA,** Cumming RG. Systematic review of randomized trials of the effect of exercise on bone mass in pre- and postmenopausal women. *Calcif Tissue Int* 2000; **67**: 10-18 [PMID: 10908406]
 - 56 **Gillespie LD,** Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, Lamb SE. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012; **9**: CD007146 [PMID: 22972103 DOI: 10.1002/14651858.CD007146.pub3]
 - 57 **Kannus P.** Preventing osteoporosis, falls, and fractures among elderly people. Promotion of lifelong physical activity is essential. *BMJ* 1999; **318**: 205-206 [PMID: 9915707]
 - 58 **Poses RM.** Medtronic settles, yet again. *Health Care Renewal*, 2011. Available from: URL: <http://hcrenewal.blogspot.com.es/2011/12/medtronic-settles-yet-again.html>
 - 59 **Tanne JH.** US makers of joint replacements are fined for paying surgeons to use their devices. *BMJ* 2007; **335**: 1065 [PMID: 18033905]
 - 60 **Lenzer J.** Editor earned over \$20m in royalties and \$2m in fees from device manufacturer. *BMJ* 2010; **340**: c495 [DOI: 10.1136/bmj.c495]
 - 61 **Sambrook P,** Stenmark J. The pharmaceutical industry and disease mongering. Authors were incorrect in their comments about Osteoporosis Australia. *BMJ* 2002; **325**: 216; author reply 216 [PMID: 12143859]
 - 62 **Santesso N,** Carrasco-Labra A, Brignardello-Petersen R. Hip protectors for preventing hip fractures in older people. *Cochrane Database Syst Rev* 2014; **3**: CD001255 [PMID: 24687239 DOI: 10.1002/14651858.CD001255.pub5]
 - 63 **Richards JB,** Rivadeneira F, Inouye M, Pastinen TM, Soranzo N, Wilson SG, Andrew T, Falchi M, Gwilliam R, Ahmadi KR, Valdes AM, Arp P, Whittaker P, Verlaan DJ, Jhamai M, Kumanduri V, Moorhouse M, van Meurs JB, Hofman A, Pols HA, Hart D, Zhai G, Kato BS, Mullin BH, Zhang F, Deloukas P, Uitterlinden AG, Spector TD. Bone mineral density, osteoporosis, and osteoporotic fractures: a genome-wide association study. *Lancet* 2008; **371**: 1505-1512 [PMID: 18455228 DOI: 10.1016/S0140-6736(08)60599-1]
 - 64 **van Dijk FS,** Zillikens MC, Micha D, Riessland M, Marcelis CL, de Die-Smulders CE, Milbradt J, Franken AA, Harsevoort AJ, Lichtenbelt KD, Pruijs HE, Rubio-Gozalbo ME, Zwertbroek R, Moutaouakil Y, Egthuisen J, Hammerschmidt M, Bijman R,

- Semeins CM, Bakker AD, Everts V, Klein-Nulend J, Campos-Obando N, Hofman A, te Meerman GJ, Verkerk AJ, Uitterlinden AG, Maugeri A, Sistermans EA, Waisfisz Q, Meijers-Heijboer H, Wirth B, Simon ME, Pals G. PLS3 mutations in X-linked osteoporosis with fractures. *N Engl J Med* 2013; **369**: 1529-1536 [PMID: 24088043 DOI: 10.1056/NEJMoa1308223]
- 65 Human Genome Project. [updated 2015 Oct 1]. Available from: URL: <http://www.genome.gov/10001772>
- 66 Downtime for hardware maintenance. [updated 2012 Dec 6]. Available from: URL: <http://hapmap.ncbi.nlm.nih.gov/>
- 67 The National Human Genome Research Institute -NHGRI-, Catalog of Publisher Genome-Wide Association Studies. [updated 2015 May 12]. Available from: URL: <http://www.genome.gov/gwastudies/>
- 68 The 1000 Genomes Project. [updated 2015 Sept 30]. Available from: URL: <http://www.1000genomes.org/>
- 69 The UK10K Project. [updated 2014 Feb 20]. Available from: URL: <http://www.1000genomes.org/announcements/1000-genomes-project-and-beyond>
- 70 Alemán A, Garcia-Garcia F, Salavert F, Medina I, Dopazo J. A web-based interactive framework to assist in the prioritization of disease candidate genes in whole-exome sequencing studies. *Nucleic Acids Res* 2014; **42**: W88-W93 [PMID: 24803668 DOI: 10.1093/nar/gku407]
- 71 Cirulli ET, Goldstein DB. Uncovering the roles of rare variants in common disease through whole-genome sequencing. *Nat Rev Genet* 2010; **11**: 415-425 [PMID: 20479773 DOI: 10.1038/nrg2779]
- 72 Gleason RP, Schneider LS. Carbamazepine treatment of agitation in Alzheimer's outpatients refractory to neuroleptics. *J Clin Psychiatry* 1990; **51**: 115-118 [PMID: 1968457 DOI: 10.1038/nature08250]
- 73 Choi M, Scholl UI, Ji W, Liu T, Tikhonova IR, Zumbo P, Nayir A, Bakkaloglu A, Ozen S, Sanjad S, Nelson-Williams C, Farhi A, Mane S, Lifton RP. Genetic diagnosis by whole exome capture and massively parallel DNA sequencing. *Proc Natl Acad Sci USA* 2009; **106**: 19096-19101 [PMID: 19861545 DOI: 10.1073/pnas.0910672106]
- 74 Wang Z, Gerstein M, Snyder M. RNA-Seq: a revolutionary tool for transcriptomics. *Nat Rev Genet* 2009; **10**: 57-63 [PMID: 19015660 DOI: 10.1038/nrg2484]
- 75 de Klerk E, 't Hoen PA. Alternative mRNA transcription, processing, and translation: insights from RNA sequencing. *Trends Genet* 2015; **31**: 128-139 [PMID: 25648499 DOI: 10.1016/j.tig.2015.01.001]
- 76 Chu Y, Corey DR. RNA sequencing: platform selection, experimental design, and data interpretation. *Nucleic Acid Ther* 2012; **22**: 271-274 [PMID: 22830413 DOI: 10.1089/nat.2012.0367]
- 77 Mårtson A, Kōks S, Reimann E, Prans E, Erm T, Maasalu K. Transcriptome analysis of osteosarcoma identifies suppression of wnt pathway and up-regulation of adiponectin as potential biomarker. *Genomic Discovery* 2013; **1**: 1-9 [DOI: 10.7243/2052-7993-1-1]
- 78 Grimes R, Jepsen KJ, Fitch JL, Einhorn TA, Gerstenfeld LC. The transcriptome of fracture healing defines mechanisms of coordination of skeletal and vascular development during endochondral bone formation. *J Bone Miner Res* 2011; **26**: 2597-2609 [PMID: 21826735 DOI: 10.1002/jbmr.486]
- 79 Nicholson JK, Lindon JC. Systems biology: Metabonomics. *Nature* 2008; **455**: 1054-1056 [PMID: 18948945 DOI: 10.1038/4551054a]
- 80 Deepinder F, Chowdary HT, Agarwal A. Role of metabolomic analysis of biomarkers in the management of male infertility. *Expert Rev Mol Diagn* 2007; **7**: 351-358 [PMID: 17620044]
- 81 Courant F, Antignac JP, Monteau F, Le Bizec B. Metabonomics as a potential new approach for investigating human reproductive disorders. *J Proteome Res* 2013; **12**: 2914-2920 [PMID: 23651426 DOI: 10.1021/pr400204q]
- 82 Kovac JR, Pastuszak AW, Lamb DJ. The use of genomics, proteomics, and metabolomics in identifying biomarkers of male infertility. *Fertil Steril* 2013; **99**: 998-1007 [PMID: 23415969 DOI: 10.1016/j.fertnstert.2013.01.111]
- 83 Tomlins AM, Foxall PJ, Lynch MJ, Parkinson J, Everett JR, Nicholson JK. High resolution 1H NMR spectroscopic studies on dynamic biochemical processes in incubated human seminal fluid samples. *Biochim Biophys Acta* 1998; **1379**: 367-380 [PMID: 9545599]
- 84 Groenen PM, Engelke UF, Wevers RA, Hendriks JC, Eskes TK, Merkus HM, Steegers-Theunissen RP. High-resolution 1H NMR spectroscopy of amniotic fluids from spina bifida fetuses and controls. *Eur J Obstet Gynecol Reprod Biol* 2004; **112**: 16-23 [PMID: 14687733]
- 85 Ellis DI, Goodacre R. Metabolic fingerprinting in disease diagnosis: biomedical applications of infrared and Raman spectroscopy. *Analyst* 2006; **131**: 875-885 [PMID: 17028718]
- 86 Griffin JL. Metabonomics: NMR spectroscopy and pattern recognition analysis of body fluids and tissues for characterisation of xenobiotic toxicity and disease diagnosis. *Curr Opin Chem Biol* 2003; **7**: 648-654 [PMID: 14580571]
- 87 Moestue S, Sitter B, Bathen TF, Tessem MB, Gribbestad IS. HR MAS MR spectroscopy in metabolic characterization of cancer. *Curr Top Med Chem* 2011; **11**: 2-26 [PMID: 20809888]
- 88 Martínez-Bisbal MC, Monleon D, Assemat O, Piotta M, Piquer J, Llácer JL, Celda B. Determination of metabolite concentrations in human brain tumour biopsy samples using HR-MAS and ERETIC measurements. *NMR Biomed* 2009; **22**: 199-206 [PMID: 18833546 DOI: 10.1002/nbm.1304]
- 89 Righi V, Roda JM, Paz J, Mucci A, Tugnoli V, Rodriguez-Tarduch G, Barrios L, Schenetti L, Cerdán S, Garcia-Martin ML. 1H HR-MAS and genomic analysis of human tumor biopsies discriminate between high and low grade astrocytomas. *NMR Biomed* 2009; **22**: 629-637 [PMID: 19322812 DOI: 10.1002/nbm.1377]
- 90 Sitter B, Sonnewald U, Spraul M, Fjøsne HE, Gribbestad IS. High-resolution magic angle spinning MRS of breast cancer tissue. *NMR Biomed* 2002; **15**: 327-337 [PMID: 12203224]
- 91 Sitter B, Lundgren S, Bathen TF, Halgunset J, Fjosne HE, Gribbestad IS. Comparison of HR MAS MR spectroscopic profiles of breast cancer tissue with clinical parameters. *NMR Biomed* 2006; **19**: 30-40 [PMID: 16229059]
- 92 Bathen TF, Sitter B, Sjøbakk TE, Tessem MB, Gribbestad IS. Magnetic resonance metabolomics of intact tissue: a biotechnological tool in cancer diagnostics and treatment evaluation. *Cancer Res* 2010; **70**: 6692-6696 [PMID: 20699363 DOI: 10.1158/0008-5472.CAN-10-0437]
- 93 Chan EC, Koh PK, Mal M, Cheah PY, Eu KW, Backshall A, Cavill R, Nicholson JK, Keun HC. Metabolic profiling of human colorectal cancer using high-resolution magic angle spinning nuclear magnetic resonance (HR-MAS NMR) spectroscopy and gas chromatography mass spectrometry (GC/MS). *J Proteome Res* 2009; **8**: 352-361 [PMID: 19063642 DOI: 10.1021/pr8006232]
- 94 Levin YS, Albers MJ, Butler TN, Spielman D, Peehl DM, Kurhanewicz J. Methods for metabolic evaluation of prostate cancer cells using proton and (13)C HR-MAS spectroscopy and [3-(13)C] pyruvate as a metabolic substrate. *Magn Reson Med* 2009; **62**: 1091-1098 [PMID: 19780158 DOI: 10.1002/mrm.22120]
- 95 Stenman K, Stattin P, Stenlund H, Riklund K, Gröbner G, Bergh A. H RMAS NMR Derived Bio-markers Related to Tumor Grade, Tumor Cell Fraction, and Cell Proliferation in Prostate Tissue Samples. *Biomark Insights* 2011; **6**: 39-47 [PMID: 21499438 DOI: 10.4137/BMI.S6794]
- 96 Swanson MG, Vigneron DB, Tabatabai ZL, Males RG, Schmitt L, Carroll PR, James JK, Hurd RE, Kurhanewicz J. Proton HR-MAS spectroscopy and quantitative pathologic analysis of MRI/3D-MRSI-targeted postsurgical prostate tissues. *Magn Reson Med* 2003; **50**: 944-954 [PMID: 14587005]
- 97 Borgan E, Sitter B, Lingjærde OC, Johnsen H, Lundgren S, Bathen TF, Sørliie T, Børresen-Dale AL, Gribbestad IS. Merging transcriptomics and metabolomics--advances in breast cancer profiling. *BMC Cancer* 2010; **10**: 628 [PMID: 21080935 DOI: 10.1186/1471-2407-10-628]
- 98 Moynihan R, Nickel B, Hersch J, Doust J, Barratt A, Beller E, McCaffery K. What do you think overdiagnosis means? A qualitative analysis of responses from a national community survey of Australians. *BMJ Open* 2015; **5**: e007436 [PMID: 25991454 DOI: 10.1136/bmjopen-2014-007436]
- 99 Moynihan R, Nickel B, Hersch J, Beller E, Doust J, Compton

Guerado E *et al.* Hip fractures are not caused by osteoporosis

S, Barratt A, Bero L, McCaffery K. Public Opinions about Overdiagnosis: A National Community Survey. *PLoS One* 2015; **10**: e0125165 [PMID: 25992887 DOI: 10.1371/journal.pone.0125165]
100 **DeFrank JT**, Barclay C, Sheridan S, Brewer NT, Gilliam M,

Moon AM, Rearick W, Ziemer C, Harris R. The psychological harms of screening: the evidence we have versus the evidence we need. *J Gen Intern Med* 2015; **30**: 242-248 [PMID: 25150033 DOI: 10.1007/s11606-014-2996-5]

P- Reviewer: La Montagna G, Lee YK, Kovar FM, Sebestyén A
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Wu HL



Elbow ulnar collateral ligament injuries in athletes: Can we improve our outcomes?

Lauren H Redler, Ryan M Degen, Lucas S McDonald, David W Altchek, Joshua S Dines

Lauren H Redler, Ryan M Degen, Lucas S McDonald, David W Altchek, Joshua S Dines, Sports Medicine and Shoulder Service, Hospital for Special Surgery, New York, NY 10021, United States

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: No potential conflicts of interest. No financial support.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Lauren H Redler, MD, Sports Medicine and Shoulder Service, Hospital for Special Surgery, 535 E 70th St, New York, NY 10021, United States. lauren.redler@gmail.com
 Telephone: +1-203-5439376

Received: September 29, 2015
 Peer-review started: October 7, 2015
 First decision: November 4, 2015
 Revised: November 18, 2015
 Accepted: January 5, 2016
 Article in press: January 7, 2016
 Published online: April 18, 2016

Abstract

Injury to the ulnar collateral ligament (UCL) most commonly occurs in the overhead throwing athlete. Knowledge surrounding UCL injury pathomechanics

continues to improve, leading to better preventative treatment strategies and rehabilitation programs. Conservative treatment strategies for partial injuries, improved operative techniques for reconstruction in complete tears, adjunctive treatments, as well as structured sport specific rehabilitation programs including resistive exercises for the entire upper extremity kinetic chain are all important factors in allowing for a return to throwing in competitive environments. In this review, we explore each of these factors and provide recommendations based on the available literature to improve outcomes in UCL injuries in athletes.

Key words: Elbow; Ulnar collateral ligament; Valgus instability; Tommy John surgery; Rehabilitation; Overhead athlete; Improved outcomes

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: While surgical techniques undoubtedly affect the outcome following ulnar collateral ligament (UCL) reconstruction, they do not independently do so. Rather, it is a complex milieu of pre-operative, intra-operative, and post-operative factors that combine to affect the overall outcome following UCL injury. Due to the variability in success rates for treatment of these injuries, careful review of each of these factors is required to ensure outcomes are optimized following treatment. This study serves as a review of these factors, providing recommendations based on available literature to improve outcomes following UCL injuries in athletes in future years.

Redler LH, Degen RM, McDonald LS, Altchek DW, Dines JS. Elbow ulnar collateral ligament injuries in athletes: Can we improve our outcomes? *World J Orthop* 2016; 7(4): 229-243 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/229.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.229>

INTRODUCTION

Ulnar collateral ligament (UCL) injuries have occurred with an increasing incidence among throwing athletes in recent years^[1]. Once considered a career-ending injury, Dr. Jobe’s reconstructive technique revolutionized the treatment of these injuries, improving outcomes and return-to-sport following surgical reconstruction^[2]. Since that time, attention has focused on optimizing the surgical technique, with several subsequent modifications aimed at improving outcomes and minimizing associated complication rates. While seemingly successful based on summative analyses in recent systematic reviews^[3,4], the results are inconsistent, with return to play rates varying from 53%-90%^[5-9] and complication rates varying from 3%-25%^[10,11]. This disparity in outcomes following surgical reconstruction has prompted further study into the management of UCL injuries beyond advancements in surgical techniques. Consequently, knowledge surrounding UCL injury pathomechanics continues to improve, leading to better preventative treatment strategies and rehabilitation programs^[1,12,13]. Additionally, the role of rigorous post-operative rehabilitation programs is a significant contributing factor to successful return-to-sport following surgical reconstruction^[14,15].

While surgical techniques undoubtedly affect the outcome following UCL reconstruction, they do not independently do so. Rather, it is a complex milieu of pre-operative, intra-operative, and post-operative factors that combine to affect the overall outcome following UCL injury. Due to the variability in success rates for treatment of these injuries, careful review of each of these factors is required to ensure outcomes are optimized following treatment. This study serves as a review of these factors, providing recommendations based on available literature to improve outcomes following UCL reconstruction in future years (Table 1).

NON-RECONSTRUCTIVE OPTIONS

Throwing athletes who have sustained UCL injuries often require surgical reconstruction in order to return to their preinjury level of activity. There are, however, non-operative and non-reconstructive modalities that may be utilized in certain clinical scenarios permitting earlier return to sport without the morbidity associated with reconstruction.

Non-operative treatment can include rest, non-steroidal anti-inflammatory drugs (NSAIDs), and bracing along with physical therapy. Rettig *et al*^[16] described a 2-phase non-operative rehabilitation program. Phase 1, typically 2 to 3 mo in duration, consisted of rest, bracing, NSAIDs and progressive range of motion (ROM) exercises. If pain-free at the end of this phase continued, strengthening and throwing progression programs were started. In some scenarios involving lifting or throwing, bracing was used to prevent elbow hyperextension. With this protocol, they had success in

Table 1 Key factors for improving outcomes in ulnar collateral ligament injuries at various time points

Time point	Target points for improved outcomes
Pre-op	Patient selection
Intra-op	Do not transpose nerve unless symptoms present preoperatively
Post-op	Docking > Jobe (complications)
	Sport specific rehabilitation
	Isokinetic testing
	Return to throw program
	Daily stretching exercises

returning 42% of throwing athletes to their pre-injury level of activity at an average of 24.5 wk^[16]. Additional non-operative measures include activity modifications, which may include sport cessation or a position change, allowing continued participation without surgical treatment. Beyond these non-operative measures, additional non-reconstructive treatment options include platelet-rich plasma (PRP) treatment or primary repair of the UCL.

PRP use has increased substantially for treatment of various tendon and ligament pathology, however little literature exists on its use specifically in UCL injuries. A recent retrospective review by Dines *et al*^[17] examined 44 baseball players treated for partial thickness UCL injuries with PRP. Levels of participation varied from professional (6), collegiate (14) and high-school (24). Though a small cohort, outcomes following treatment with PRP were best in the professional group with 67% returning to play^[17]. Only 36% of the collegiate athletes and 17% of the high school athletes had excellent outcome scores based on a modified Conway Scale^[17]. Overall these outcomes are worse than UCL reconstruction and should be reserved for specific patient groups. One such group may include athletes who are late in their professional careers and unable to undergo necessary post-operative rehabilitation. Return to pitching following reconstruction requires 12+ mo of post-operative rehabilitation, while return from non-operative treatment with PRP is significantly shorter, based on the ability to progress through an interval-throwing program. Therefore, these older overhead athletes may receive the most benefit from a PRP injection following partial UCL injury^[18].

While PRP may have a positive effect on UCL healing, corticosteroids have a negative effect on ligament healing and are not recommended for use following acute ligamentous injuries. Using a rabbit model, Walsh *et al*^[19] injected betamethasone into a surgically created UCL defects, reporting negative effects on both biomechanical and histologic properties of the healing ligament. As a result of the deleterious effects on ligamentous healing, corticosteroids are not recommended in the treatment of acute UCL injuries^[19].

Primary repair of the UCL, rather than reconstruction, may permit more rapid return to play and

improved outcomes in specific patient groups^[20,21]. Younger athletes who sustain UCL injuries have a distinct injury pattern from professional athletes that is more amenable to repair, typically confined to either the proximal and/or distal aspect of the UCL rather than a degenerative mid-substance injury attributable to repetitive micro-trauma^[20,21]. In 2008, Savoie *et al.*^[21] reported the outcomes of primary repair of UCL injuries in patients averaging 17.2 years of age, with nearly 5 years of follow-up. Through their work, they identified that the best candidate for this treatment type is one with an acute avulsion injury without signs of previous degenerative injury and no noted concomitant injuries. Their described technique includes a diagnostic arthroscopy for confirmation of pathology, followed by a muscle-splitting approach^[22] with capsular reflection along the anterior edge of the ligament permitting evaluation of intra-articular damage. Anatomic repair is performed using bone tunnels or a double loaded anchor, securing the injured ligament proximally at the base of the medial epicondyle or distally at the center of the sublime tubercle^[21].

Post-operative rehabilitation includes splinting followed by full time hinged ROM brace wear and an expedited standard rehabilitation protocol^[15]. Progressive return to play was permitted in an ROM brace at 6-8 wk post-operatively with progression out of the brace at 12 wk with return to full activities upon graduation from the return to play program at 16 to 24 wk post-operatively^[21]. Results for primary repair in this specific patient cohort were excellent with 93% (56 of 60) patients returning to sporting activities within 6 mo. This included 40 patients with proximal UCL repairs, 11 with distal UCL repairs and 9 with combined proximal and distal UCL repairs^[21].

The results of Savoie *et al.*^[21] are similar to results of primary repair reported by Richard *et al.*^[20] in a collegiate patient population with an average age of 27 who sustained combined acute UCL and flexor-pronator avulsion from the humeral origin. Of the 11 patients who underwent primary repair through bone tunnel fixation, 9 returned to collegiate athletics between 4 and 6 mo post-operatively^[20]. Though this study is limited by short, 16-mo follow-up and a wider variety of sporting activities with fewer overhead athletes, it illustrates a patient population that may benefit from primary UCL repair.

Both of these studies' outcomes differ from earlier results from Conway *et al.*^[10] who reported outcomes for patients treated with either UCL repair or reconstruction. In their study of throwing athletes only 50% of patients undergoing a direct repair returned to their previous level of sport compared to 68% of those undergoing a reconstruction^[10]. Even worse outcomes were obtained in major-league baseball players undergoing primary repair with only 2 of the 7 being able to return to sport^[10].

In short, UCL repair may be a viable surgical

option in young athletes with acute injuries, resulting in excellent outcomes and permitting earlier return to play than following UCL reconstruction. This procedure, however, should be limited to young athletes without degenerative UCL injuries as is often encountered in collegiate and professional baseball players.

RECONSTRUCTIVE OPTIONS

Ulnar collateral ligament reconstruction has been effective in returning athletes to sport in approximately 80% of cases^[3]. However, the results differ widely depending on the surgical series, with highly variable return-to-play rates (as low as 53%) and complication rates (as high as 25%), often related to the specific reconstructive techniques. In addition, studies have identified significantly inferior functional outcomes among those who re-tear their UCL and require revision UCL reconstruction, with a return to play rate ranging from 33%-78%^[23-25]. Due to the variability in achieving a successful outcome following UCL reconstruction, and the ramifications of re-injury and revision surgery, careful review of surgical techniques is necessary to ensure that appropriate surgical steps are taken to optimize outcomes and limit complication and re-rupture rates.

Surgical techniques

Surgical reconstruction of the UCL was first described by Dr. Frank Jobe in 1986. His primary reconstructive method involved detachment of the flexor-pronator musculature, submuscular transposition of the ulnar nerve and reconstruction of the UCL with a palmaris longus or plantaris tendon graft in a figure-8 configuration with repair of the flexor-pronator tenotomy^[2]. The first successful procedure was performed on pitcher Tommy John in 1974. In Jobe's initial series of 16 patients he reported a return-to-play rate of 63%, with a complication rate of 32%, most commonly related to ulnar neuropathy^[2]. In a follow-up series of 71 patients using the same reconstruction method, he noted 68% return to sport with a 21% complication rate^[10].

While offering an improved outcome compared with conservative treatment or acute UCL repair, concern remained over the relatively high complication rate associated with Jobe's reconstructive method^[10]. As a result, the modified Jobe technique was subsequently described by Smith *et al.*^[22], who introduced a flexor-pronator muscle-splitting approach that obviated the need for an obligatory ulnar nerve transposition and avoided tenotomizing the flexor-pronator origin. This modification resulted in an excellent outcome in 93% of a series of 83 athletes, with a 100% return to play rate^[26]. Complications were reported in 5% and were limited to transient ulnar neuropathy, which resolved in all patients. It should be noted that while this approach no longer required a submuscular ulnar nerve transposition, many surgeons continue

to perform subcutaneous ulnar nerve transpositions with the modified Jobe technique in select cases with preceding ulnar nerve symptoms, or routinely in all cases, depending on individual preference. Cain *et al*^[27] reported on the outcomes of 743 patients that underwent UCL reconstruction utilizing the modified Jobe reconstruction with concomitant subcutaneous ulnar nerve transpositions. They identified an 83% return-to-play rate, and 20% complication rate. Notably, the authors of this study reported re-operation rates of 19% for residual posteromedial impingement.

As experience continued to grow in treating these injuries, concern was raised over the method of graft tensioning and fixation using the figure-of-8 configuration. Subsequently, Rohrbough *et al*^[9] introduced a reconstruction method known as the docking technique to reduce the size of the humeral tunnels and improve fixation strength of the reconstruction. This procedure is performed through a muscle-splitting approach and does not require ulnar nerve transposition. It also involves looping the graft through a similar bone tunnel in the proximal ulna, however it differs in that both free limbs of the graft are then passed into a single tunnel on the humerus, with sutures exiting posteriorly through smaller drill holes, allowing the sutures to be tied over a posterior bony bridge. In addition, authors recommended routine elbow arthroscopy to treat concomitant pathology in the elbow joint, which was noted in up to 45% of patients^[9]. In their index cohort of 36 patients, they reported a 92% return-to-play rate at the same level of competition, with only a 5.5% complication rate, including one transient ulnar neuropathy and one wound hematoma^[9]. A larger follow-up study of 100 patients over 3 years revealed a 90% return to play rate, with only a 3% complication rate. Similarly, Paletta *et al*^[28] described a modified docking technique utilizing a quadrupled, rather than doubled, palmaris graft, with slight differences in humeral bone tunnel preparation. Their procedure offered similar outcomes with 92% return to pre-injury level of competition, with slightly higher complication rates of 8%^[28]. Additionally, Bowers *et al*^[29] treated 21 overhead athletes with a modified docking technique using a triple-strand Palmaris graft. They had 19 (90%) excellent results, 2 good results, and no complications^[29].

An additional modification attempted to address the inability of reconstruction techniques to restore the biomechanical strength comparable to the native ligament. Ahmad *et al*^[30] identified improved fixation strength with cadaveric testing of a reconstructive technique using interference screw fixation, resulting in the development of a hybrid technique with ulnar interference screw fixation and humeral docking, known as the DANE TJ technique^[31]. Otherwise, the procedure was unchanged, performed through a flexor-pronator muscle-splitting approach without ulnar nerve transposition. Results from the initial technique description, reported 86% return-to-play rates,

with 18% complication rate of either transient ulnar neuropathy (9%) or post-operative adhesions requiring re-operation (9%)^[31].

With many of these surgical techniques, there is concern over the size of the bone tunnels and the effect on graft tensioning and the potential for bone bridge compromise. A recent biomechanics study on 10 cadaveric elbows investigated the relationship graft size had on resistance to valgus load^[32]. They found no significant difference in angular valgus deformation between palmaris longus, triceps brachii, extensor carpi radialis longus, and semitendinosus.

Further review of all available surgical technique descriptions and clinical series on UCL reconstructions was performed in two recent systematic reviews, which allowed for pooling of data to provide further comparative analysis between the different surgical techniques^[3,4]. In the first review, Vitale *et al*^[3] reported outcomes associated with different aspects of each surgical approach. They report that transitioning from a flexor-pronator detachment to a muscle-splitting surgical approach improved the success rates from 70% to 87%, while also reducing the rate of post-operative ulnar neuropathy from 20% to 6%. Additionally, adoption of the muscle-splitting approach reduced the need for an obligatory ulnar nerve transposition. Outcomes were noted to improve from a success rate of 75% in those who had an obligatory transfer to 89% in those who did not. Also, those undergoing an obligatory nerve transfer had a 9% rate of post-operative ulnar neuropathy, while only 4% of those who did not undergo a transposition reported the same. Finally, adoption of the docking and modified docking techniques also significantly improved outcomes with 90% and 95% of patients reporting excellent outcomes with these respective techniques, compared with only 76% of those undergoing reconstruction with the figure-of-8 technique. Similarly, a decrease in post-operative ulnar neuropathy rates was also noted among those undergoing docking and modified docking reconstructions compared with the figure-of-8 technique, with only 3% and 5% experiencing these complications in the docking groups while 8% of those with the figure-of-8 technique were observed to experience this complication.

A second systematic review by Watson *et al*^[4] provided a comparison of the overall complication rates associated with each reconstructive technique. Cumulatively, when considering all reported outcomes from UCL reconstruction clinical series, they identified a complication rate of 16.6%, with the majority of these complications being ulnar neuropathy (12.9%). Further stratification of these results revealed different rates dependent on procedure, with the original Jobe reconstruction carrying a complication rate of 29.2%, while the modified Jobe technique carried a complication rate of 19.1%. The docking technique and

modified docking technique had lower rates of 6% and 4.3% respectively.

Based on the results of these reported series and systematic analyses, it appears that newer reconstructive methods, including the docking and modified docking procedures, are associated with higher return-to-play rates and lower complication rates than earlier techniques, including the Jobe and modified Jobe techniques, as well as in comparison to the DANE TJ technique. Additionally, it appears that use of a muscle splitting surgical approach, without obligate ulnar nerve transposition, is also associated with improved outcome rates and lower complication rates. Finally, consideration should be given to both open or arthroscopic assessment and treatment of concomitant pathology, specifically posteromedial impingement, which was treated in 34%-45% of cases in larger volume series^[3,11,27]. While no randomized trial exists to corroborate these conclusions, they are based on the best-available literature, including clinical data from over 1300 patients.

Adjunctive treatments

In addition to modifications in surgical techniques, basic science research is ongoing to determine if there are any adjunctive therapies that may expedite or improve the quality of tendon-to-bone healing following UCL reconstruction. As identified in both ACL reconstruction and rotator cuff repair surgery, the structure and composition of the insertion site is complex, with a gradual transition from tendon to bone with interposed unmineralized and mineralized fibrocartilage^[33,34]. This architecture is typically not reconstituted in the normal healing process following ligament reconstruction or rotator cuff repair, although several attempts have been made at adding biologic agents to stimulate regenerative, rather than reparative, healing in both ACL and rotator cuff injuries.

For ACL injuries, addition of a collagen-platelet rich plasma scaffold following direct ligament repair was found to improve biomechanical and histologic properties of the healing ligament in both animals and humans^[35,36]. Application of PRP following ACL reconstruction in animal models has also shown positive results in stimulating revascularization and re-innervation of the ACL graft^[37,38]. Clinical results of PRP addition following ACL reconstruction have been less impressive, with only mild or no clinical improvement noted^[39,40]. Similarly, stem cell use has also been studied in conjunction with ACL reconstruction, where addition of tendon-derived stem cell sheets and bioengineered periosteal progenitor cell sheets have demonstrated encouraging results in small animal models with improved fibrocartilage and bone formation at the tendon-bone junction, although clinical results are limited due to restrictions regarding stem cell utilization^[41,42].

While there is a paucity of literature on the effect of these various orthobiologic agents in UCL reconstruction,



Figure 1 Modified sleeper stretch. The athlete lies on her side with her scapula retracted, rotates slightly posteriorly to place the shoulder in the scapular plane (dashed line), and passively internally rotates the shoulder until a mild stretch is felt. Hold for 30 s, relax, and repeat 3 times.

results of the literature for both ACL reconstruction and rotator cuff repair can potentially be extrapolated to this group. Further study is necessary to see if these biologic agents can potentially improve or expedite healing to allow for improved clinical outcomes and lower re-injury rates.

POST-OPERATIVE

Every athlete who is evaluated for an ulnar collateral ligament injury should have a thorough evaluation of all intrinsic and extrinsic factors that can contribute to valgus instability. It is important to address poor mechanics related to underlying factors, including capsular stiffness in glenohumeral internal rotation deficit (GIRD), scapular dyskinesis, and deficiencies of core and single leg strength. Post-operative and nonsurgical treatment are related to the restoration of normal scapulohumeral rhythm, which begins with establishing trunk and core stability, elbow range of motion and strength, as well as using triplanar exercises, including lunges and balance exercises^[43].

GIRD should be evaluated by stabilizing the scapula, placing the arm in 90° of abduction in the scapular plane, and internally and externally rotating the arm. Bilateral measurements should be obtained, and treatment initiated if the side-to-side difference in the total arc of rotational motion is greater than 5°^[44]. Modified sleeper stretches and modified side-lying



Figure 2 Modified side-lying cross body stretch. The athlete lies on the affected shoulder and stabilizes the scapula by rotating posteriorly (dashed line) against the table as the shoulder is horizontally adducted (arrow). External rotation is restricted *via* counter pressure of the opposite forearm. Hold for 30 s, relax, and repeat 3 times.

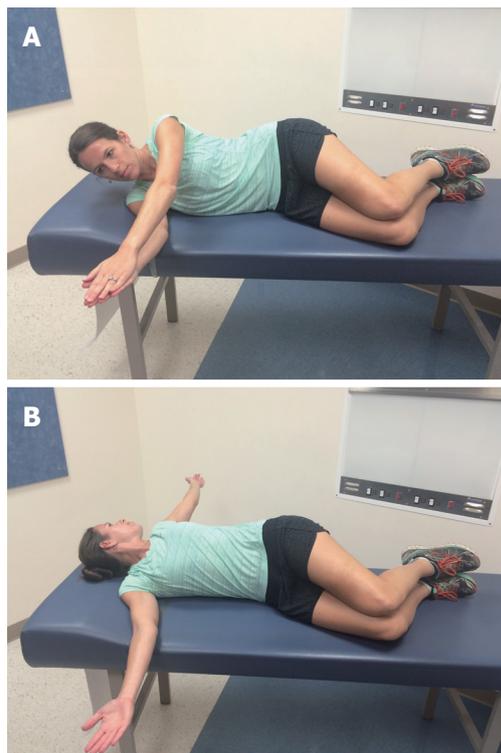


Figure 3 Open book stretch. A: The athlete lies on the unaffected shoulder with hips and knees bent 90° and arms straight out in front of him; B: Opening the chest and laying the affected extremity on the opposite side and looking in the same direction stretches the pectoralis major and biceps short head. Hold for 90 s, relax, and repeat 3 times.

cross body are excellent for improving GIRD^[45,46]. The modified sleeper stretch is performed in the lateral position with the patient lying on the affected extremity using their unaffected arm to stretch the posterior capsule (Figure 1). The modification of rotating slightly posteriorly stabilizes the scapula without causing subacromial impingement. The modified side-lying cross body stretch is performed in the lateral position with the athlete lying on the affected extremity, using the opposite hand to horizontally adduct the targeted shoulder (Figure 2). The opposite forearm is aligned on top and restricts external rotation of the humerus. The side-lying position stabilizes the scapula and resists scapular protraction allowing optimal stretch of the posterior shoulder. Each of these stretches are held for 30 s and repeated 3 times. There is evidence that the side-lying cross body stretch is more effective than the sleeper stretch^[45,46].

The open book and corner stretches can improve pectoralis minor and biceps short head flexibility. The open book stretch is performed in the lateral position lying on the unaffected extremity with the patient's knees bent and arms stretched out in front. Opening the chest and laying the affected extremity on the opposite side and looking in the same direction stretches the pectoralis major and biceps short head (Figure 3). The corner stretch is performed facing a corner with the shoulders abducted and elbows flexed to 90° and the



Figure 4 Corner stretch. The athlete faces a corner with the shoulders abducted, elbows flexed to 90° and slowly leans into the corner. Hold for 90 s, relax, and repeat 3 times.

athlete slowly leans into the corner (Figure 4). Each of these stretches are held for 90 s and repeated 3 times.

Table 2 Airfield surface movement indicator postoperative rehabilitation protocol following ulnar collateral ligament reconstruction with palmaris longus autograft

Time period	Phase	Goal
Day 0-7	Splinted at 90° flexion	Early healing of graft and fascial sling for nerve transposition
Weeks 1-5	Hinged elbow ROM brace	Protect healing tissues from valgus stress
Weeks 3-4	Light resistance isotonic exercises	Develop dynamic stabilization of the medial elbow
Week 6	Thrower's Ten Program	
Weeks 8-9	Progressive resistance exercises incorporated	
Week 12	Advanced Thrower's Ten Program	
Week 14	Two-hand plyometric drills	
Week 16	One-hand plyometric drills	
Week 22/24	Interval throwing program	
Week 22/24	Throwing from the mound	
Months 9-12	Return to competitive throwing	

ROM: Range of motion.

Scapular dyskinesis is characterized by loss of upward acromial rotation, excessive scapular internal rotation, and excessive scapular anterior tilt^[47]. These positions create scapular protraction, which decreases demonstrated rotator cuff strength^[48]. Evaluation of scapular dyskinesis is accomplished by observation of static position and dynamic motions. The emphasis for rehabilitation for ulnar collateral ligament injuries should start proximally and end distally. Proximal control of core stability leads to control of three-dimensional scapular motion, with a goal to achieve the position of optimal scapular function - posterior tilt, external rotation, and upward elevation^[43]. The serratus anterior functions most importantly as an external rotator of the scapula, and the lower trapezius acts as a stabilizer. Maximal rotator cuff strength is achieved from a stabilized, retracted scapula^[49]. Periscapular strengthening should be accomplished by taking advantage of the synergistic activity of proximal trunk and hip muscle activation^[49]. Exercise sets should include lawn mower pulls and low row exercises^[49].

Kinetic chain factors may be evaluated by screening methods. Hip and trunk stability can be assessed using the single leg stance and single leg squat maneuvers^[43]. In the single leg stance test, a positive Trendelenburg sign indicates gluteus medius weakness. Forward or lateral trunk tilt or rotation of the trunk around the leg in a single leg squat maneuver indicates a loss of dynamic control. Lunge and balance exercises should be incorporated into a rehabilitation program to improve trunk and core stability.

Rehabilitation programs vary institutionally and by treating physician. There is currently no validated comprehensive program. Rehabilitation following elbow injury or elbow surgery should follow a sequential and progressive multiphased approach that involves

a gradual and protected return of ROM and an extensive resistance exercise program for the entire upper extremity kinetic chain. The rehab program should include proprioceptive exercises to stimulate mechanoreceptors as well as total arm strengthening, emphasizing proximal scapular stabilization. Low-resistance, high-repetition programs promote an optimal return to uncompensated throwing.

Phase 1 involves immediate motion. Reestablishing full elbow extension, typically defined as preinjury motion, is the primary goal of early ROM activities. Another goal of this phase is to decrease pain and inflammation. Modalities including cryotherapy, high voltage stimulation, and laser therapy can be helpful. Once the acute inflammatory response has subsided, moist heat, warm whirlpool, and ultrasound may be used at the beginning of treatment to prepare the tissue for stretching^[50]. If the patient continues to have difficulty achieving full extension using ROM and mobilization techniques, a low load, long duration stretch may be performed to aid tissue elongation^[50]. Submaximal isometrics are performed initially for the elbow flexor and extensor, as well as the wrist flexor, extensor, pronator, and supinator muscle groups. Scapular strengthening and activation exercises are also initiated immediately following surgery.

Phase 2, the intermediate phase, starts when the patient exhibits full ROM with minimal pain and involves improving muscular strength and endurance and reestablishing neuromuscular control of the elbow. Particular emphasis is placed on shoulder external and internal rotation at 90° abduction. External rotation helps avoid increased strain on the medial elbow structures during the overhead throwing motion^[51] while internal rotation may create a protective varus force at the elbow^[50]. A complete upper extremity strengthening program, such as the Thrower's Ten Program, which focuses on the muscles needed for dynamic stability, should be included^[52] (Figure 5).

Phase 3 encompasses advanced strengthening in preparation for a gradual return to sport. To enter this phase, the athlete must demonstrate strength that is 70% of the contralateral extremity. The advanced Thrower's Ten Program^[53] is used at this stage and involves exercises based on the principles of coactivation, dynamic stabilization, muscular facilitation, endurance, and coordination^[53].

Phase 4, the final phase, involves an interval throwing program allowing the athlete to return to full competition. These throwing programs are sport specific and differ for golf and tennis athletes^[54]. Isokinetic testing is commonly performed at this stage to determine the readiness of the athlete for an interval throwing program^[54]. The interval throwing program has two phases, beginning with progressive long tosses and ending with throwing off the mound. The validity of this order has been questioned as some believe that long toss creates more stress at the medial elbow when

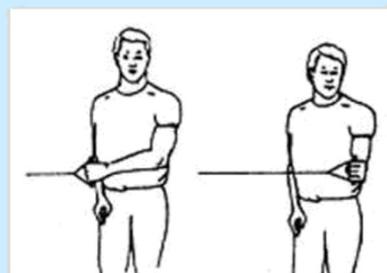
1A. Diagonal Pattern D2 Extension: Involved hand will grip tubing handle overhead and out to the side. Pull tubing down and across your body to the opposite side of leg. During the motion, lead with your thumb. Perform _____ sets of _____ repetitions _____ daily.



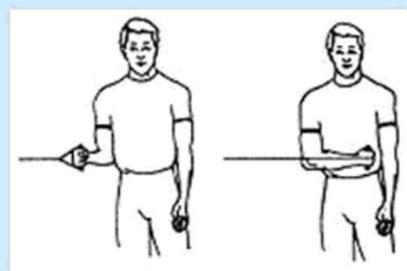
1B. Diagonal Pattern D2 Flexion: Gripping tubing handle in hand of involved arm, begin with arm out from side 45° and palm facing backward. After turning palm forward, proceed to flex elbow and bring arm up and over involved shoulder. Turn palm down and reverse to take arm to starting position. Exercise should be performed _____ sets of _____ repetitions _____ daily.



2A. External Rotation at 0° Abduction: Stand with involved elbow fixed at side, elbow at 90° and involved arm across front of body. Grip tubing handle while the other end of tubing is fixed. Pull out arm, keeping elbow at side. Return tubing slowly and controlled. Perform _____ sets of _____ repetitions _____ times daily.



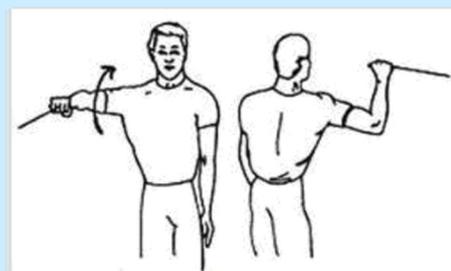
2B. Internal Rotation at 0° Abduction: Standing with elbow at side fixed at 90° and shoulder rotated out. Grip tubing handle while other end of tubing is fixed. Pull arm across body keeping elbow at side. Return tubing slowly and controlled. Perform _____ sets of _____ repetitions _____ times daily.



2C. (Optional) External Rotation at 90° Abduction: Stand with shoulder abducted 90°. Grip tubing handle while the other end is fixed straight ahead, slightly lower than the shoulder. Keeping shoulder abducted, rotate shoulder back keeping elbow at 90°. Return tubing and hand to start position.

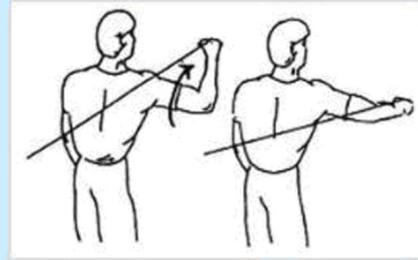
I. Slow Speed Sets: (Slow and Controlled) Perform _____ sets of _____ repetitions _____ times daily.

II. Fast Speed Sets: Perform _____ sets of _____ repetitions _____ times daily.



(continued)

2D. (Optional) Internal Rotation at 90° Abduction: Stand with shoulder abducted to 90°, externally rotated 90° and elbow bent to 90°. Keeping shoulder abducted, rotate shoulder forward, keeping elbow bent at 90°. Return tubing and hand to start position.



I. Slow Speed Sets: (Slow and Controlled) Perform _____ sets of _____ repetitions _____ times daily.

II. Fast Speed Sets: Perform _____ sets of _____ repetitions _____ times daily.

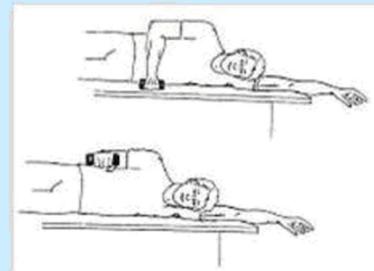
3. Shoulder Abduction to 90°: Stand with arm at side, elbow straight, and palm against side. Raise arm to the side, palm down, until arm reaches 90° (shoulder level). Perform _____ sets of _____ repetitions _____ times daily.



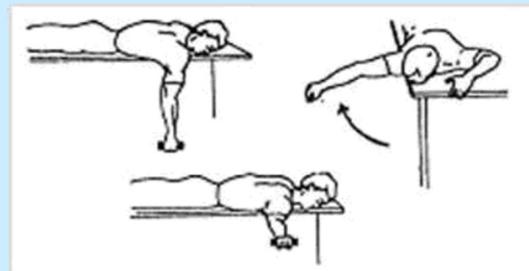
4. Scaption, External Rotation: Stand with elbow straight and thumb up. Raise arm to shoulder level at 30° angle in front of body. Do not go above shoulder height. Hold 2 seconds and lower slowly. Perform _____ sets of _____ repetitions _____ times daily.



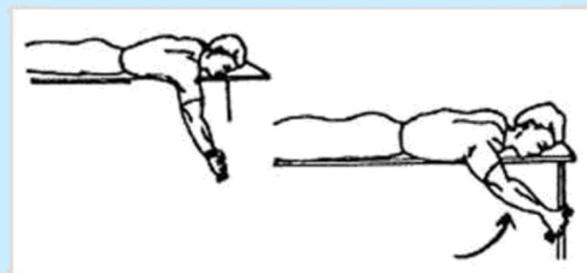
5. Sidelying External Rotation: Lie on uninvolved side, with involved arm at side of body and elbow bent to 90°. Keeping the elbow of involved arm fixed to side, raise arm. Hold seconds and lower slowly. Perform _____ sets of _____ repetitions _____ times daily.



6A. Prone Horizontal Abduction (Neutral): Lie on table, face down, with involved arm hanging straight to the floor, and palm facing down. Raise arm out to the side, parallel to the floor. Hold 2 seconds and lower slowly. Perform _____ sets of _____ repetitions _____ times daily.

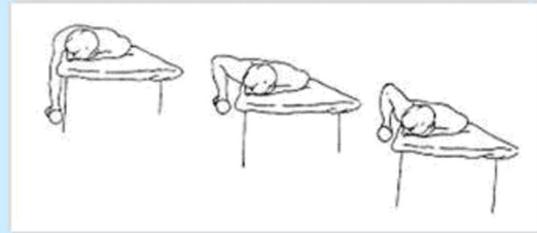


6B. Prone Horizontal Abduction (Full ER, 100° ABD): Lie on table face down, with involved arm hanging straight to the floor, and thumb rotated up (hitchhiker). Raise arm out to the side with arm slightly in front of shoulder, parallel to the floor. Hold 2 seconds and lower slowly. Perform _____ sets of _____ repetitions _____ times daily.

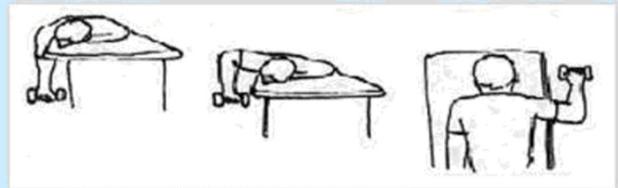


(continued)

6C. Prone Rowing: Lying on your stomach with your involved arm hanging over the side of the table, dumbbell in hand and elbow straight. Slowly raise arm, bending elbow, and bring dumbbell as high as possible. Hold at the top for 2 seconds, then slowly lower. Perform ____ sets of ____ repetitions ____ times daily.



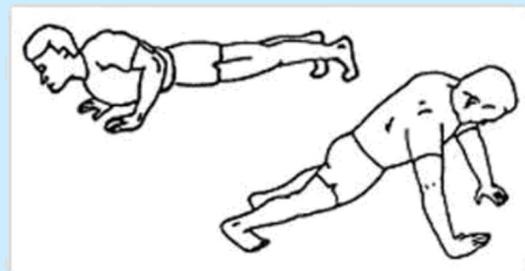
6D. Prone Rowing Into External Rotation: Lying on your stomach with your involved arm hanging over the side of the table, dumbbell in hand and elbow straight. Slowly raise arm, bending elbow, up to the level of the table. Pause one second. Then rotate shoulder upward until dumbbell is even with the table, keeping elbow at 90°. Hold at the top for 2 seconds, then slowly lower taking 2 – 3 seconds. Perform ____ sets of ____ repetitions ____ times daily.



7. Press-ups: Seated on a chair or table, place both hands firmly on the sides of the chair or table, palm down and fingers pointed outward. Hands should be placed equal with shoulders. Slowly push downward through the hands to elevate your body. Hold the elevated position for 2 seconds and lower body slowly. Perform ____ sets of ____ repetitions ____ times daily.



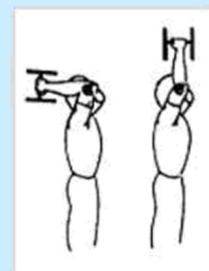
8. Push-ups: Start in the down position with arms in a comfortable position. Place hands no more than shoulder width apart. Push up as high as possible, rolling shoulders forward after elbows are straight. Start with a push-up into wall. Gradually progress to table top and eventually to floor as tolerable. Perform ____ sets of ____ repetitions ____ times daily.



9A. Elbow Flexion: Standing with arm against side and palm facing inward, bend elbow upward turning palm up as you progress. Hold 2 seconds and lower slowly. Perform ____ sets of ____ repetitions ____ times daily.



9B. Elbow Extension (Abduction): Raise involved arm overhead. Provide support at elbow from uninvolved hand. Straighten arm overhead. Hold 2 seconds and lower slowly. Perform ____ sets of ____ repetitions ____ times daily.



(continued)

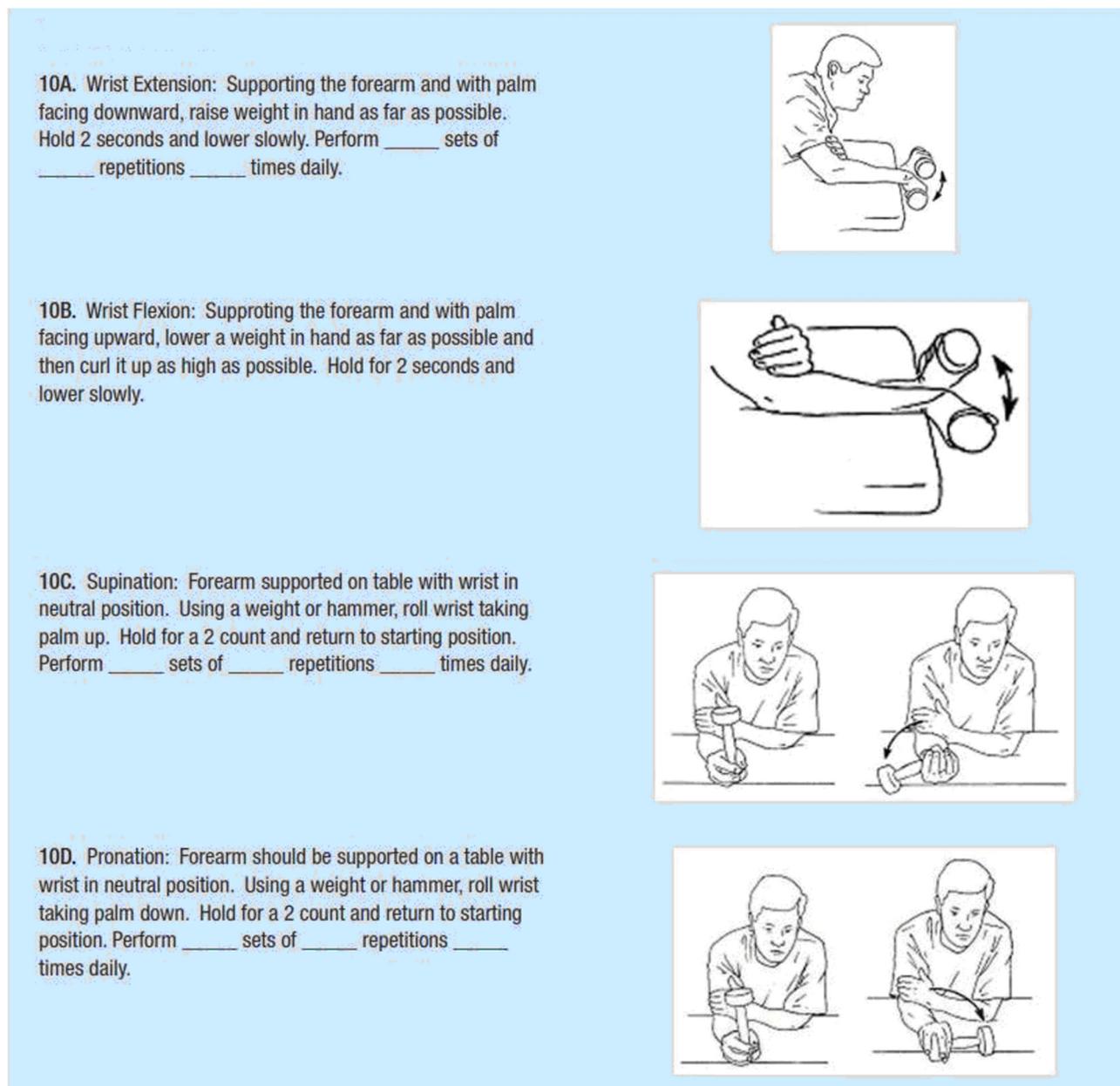


Figure 5 Thrower's ten program. The Thrower's Ten Program is designed to exercise the major muscles necessary for throwing. The Program's goal is to be an organized and concise exercise program. In addition, all exercises included are specific to the thrower and are designed to improve strength, power, and endurance of the shoulder complex musculature.

compared with off the mound throwing.

Specific postoperative rehabilitation guidelines are based on the operative technique used for UCL reconstruction. The rehabilitation program used at the Andrews Sports Medicine Institute is outlined in Table 2^[50] and the rehabilitation program used at Hospital for Special Surgery is outlined in Table 3^[50]. Dynamic stabilization of the medial elbow is accomplished by concentric and eccentric strengthening the flexor carpi ulnaris and flexor digitorum superficialis. Given their anatomic location overlying the UCL, these muscles assist the UCL in stabilizing valgus stress at the medial elbow^[50].

Injury to the UCL most commonly occurs in baseball

pitchers, but is also seen in other subsets of athletes, including javelin throwers, football quarterbacks and softball pitchers. Each sport requires different throwing mechanics and imparts different stresses to the elbow due to the varied angular velocities produced at the elbow (Table 4). Rehabilitation protocols should be sport specific and take into account the unique movements associated with these activities.

The javelin event involves throwing a 2.6-m spear weighing at least 800 g. Throwers lengthen the path of acceleration by maintaining an extended elbow for as long as possible until foot strike^[55]. The throwing motion is broken down into four phases: Approach run, cross steps, delivery stride, and thrust phase. During

Table 3 High speed steels postoperative rehabilitation protocol following ulnar collateral ligament reconstruction with palmaris longus autograft

Time period	Treatment strategies	Goal
Day 0-10	Splinted or hinged elbow ROM brace at 60 degrees flexion	Promote graft healing, reduce pain, and swelling
Weeks 1-4	Hinged elbow ROM brace at all times No PROM Elbow AROM in brace	Restore ROM 30°-90° Promote graft healing Independent home exercise program
Weeks 4-6	Continue brace wear at all times Avoid PROM Avoid valgus stress Continue AROM in brace	Restore ROM 15°-115° Minimal pain and swelling
Weeks 6-12	Isometric exercises of deltoid, wrist, elbow Minimize valgus stress Avoid PROM by the clinician Avoid pain with exercises Continue AROM	Restore full ROM All upper extremity strength 5/5 Begin to restore muscular endurance
Week 8	Low intensity, long duration stretch for extension Isotonic exercises of the scapula, shoulder, elbow, forearm and wrist Eccentric training when strength is adequate Begin internal/external rotation strengthening Begin forearm pronation/supination strengthening	
Weeks 12-16	Pain free plyometric exercises Advance internal/external rotation to 90/90 position Neuromuscular drills Plyometric program Endurance training	Restore full strength and flexibility Prepare for return to activity
Week 16	Begin interval throwing program	
Weeks 16-36	Avoid pain with throwing or hitting Avoid loss of strength or flexibility Continue flexibility training Continue strengthening program	Return to activity Prevent reinjury
Week 20	Begin hitting program	

ROM: Range of motion; AROM: Active range of motion; PROM: Passive range of motion.

Table 4 Angular velocity by sport

Sport	Baseball	Softball	Football	Javelin	Tennis
Angular velocity	2400°/s	570°/s	1760°/s	1900°/s	982°/s

the thrust phase, the elbow flexes from 40°-60°^[55]. As contrasted with baseball pitchers who undergo rapid extension, javelin throwers undergo rapid flexion. Although throwing a javelin and pitching a baseball both produce large valgus forces on the medial side of the elbow, leading to UCL injuries, the mechanics of throwing are vastly different. Perhaps there should be changes to post-operative protocols that specifically address these specialized movement differences. No consensus postoperative protocol and throwing program exists for javelin throwers in the literature. As a javelin is much heavier than a baseball (1.76 pounds vs 0.32 pounds), we prefer to wait 8 mo from surgery (as compared to 4 in baseball pitchers) to begin an interval throwing program. We also recommend focusing more on lower extremity core strengthening to account for the increased weight of the javelin. Javelin throwers should be counseled that due to their unique motion and weight of the javelin, their return to play will be longer than in baseball players, and should be expected

around 15 mo.

The motion of throwing a football is similar to throwing a baseball pitch. The lower incidence of elbow injuries in football quarterbacks is multifactorial. With a larger size ball, arm velocities are much slower, therefore producing less stress. The motion is also more over-the-top which produces less valgus force at the elbow. It is also hypothesized that the follow-through phase is abbreviated as the quarterback needs to be prepared for the impact from an opposing player, possibly lowering forces and torques produced at the elbow. Finally, quarterbacks perform the throwing motion significantly few times per game and per season compared to major league pitchers, and therefore are cumulatively placing less stress on their elbows. While some quarterback UCL injuries are chronic, the vast majority in the literature are from acute contact injuries^[56,57]. Results from Dodson *et al*^[56] and Kenter *et al*^[57] suggest that these players can be successfully treated nonoperatively and return to competitive play.

Softball pitchers are a unique subset of throwers due to the underhand nature of their motion. While the overhead thrower is extending the elbow at ball release, the underhand softball pitcher is flexing the elbow. Although reasons are unclear, the female athlete, especially the underhand softball pitcher, imparts less

stress to the elbow, making the injury more amenable to repair^[58]. There is some evidence to suggest positive outcomes in ligament reconstruction for these athletes. However, the data on these athletes lacks the data that we have for their male counterparts. Further research into female throwing injuries is necessary. Currently, repair is a viable option.

UCL injuries have also been reported tennis, gymnastics, wrestling, volleyball and in baseball position players^[27]. The demands of their sports and positions result in a much lower frequency of injury and usually do not necessitate UCL reconstruction for return to play. Further research is needed to investigate sport-specific protocols and treatment outcomes for athletes who play sports that place the UCL at risk.

CONCLUSION

We still need to answer the unknown. For example, currently we throw long-toss before mound throwing. There is some evidence to support that this actually puts more stress on the UCL reconstruction. Return to sport at the same or higher level may be easier for a high school athlete compared to a professional pitcher, but currently these are not differentiated in the literature. In order to have functional screening and quantitative return to play after UCL reconstruction like we currently have for ACL reconstruction, we need to know what is normal at every level of participation and position, including professional, college, high school athletes as well as distinctions between pitchers vs position players.

REFERENCES

- 1 **Fleisig GS**, Andrews JR. Prevention of elbow injuries in youth baseball pitchers. *Sports Health* 2012; **4**: 419-424 [PMID: 23016115 DOI: 10.1177/1941738112454828]
- 2 **Jobe FW**, Stark H, Lombardo SJ. Reconstruction of the ulnar collateral ligament in athletes. *J Bone Joint Surg Am* 1986; **68**: 1158-1163 [PMID: 3771597]
- 3 **Vitale MA**, Ahmad CS. The outcome of elbow ulnar collateral ligament reconstruction in overhead athletes: a systematic review. *Am J Sports Med* 2008; **36**: 1193-1205 [PMID: 18490476 DOI: 10.1177/0363546508319053]
- 4 **Watson JN**, McQueen P, Hutchinson MR. A systematic review of ulnar collateral ligament reconstruction techniques. *Am J Sports Med* 2014; **42**: 2510-2516 [PMID: 24220014 DOI: 10.1177/0363546513509051]
- 5 **Erickson BJ**, Gupta AK, Harris JD, Bush-Joseph C, Bach BR, Abrams GD, San Juan AM, Cole BJ, Romeo AA. Rate of return to pitching and performance after Tommy John surgery in Major League Baseball pitchers. *Am J Sports Med* 2014; **42**: 536-543 [PMID: 24352622 DOI: 10.1177/0363546513510890]
- 6 **Makhni EC**, Lee RW, Morrow ZS, Gualtieri AP, Gorroochurn P, Ahmad CS. Performance, Return to Competition, and Reinjury After Tommy John Surgery in Major League Baseball Pitchers: A Review of 147 Cases. *Am J Sports Med* 2014; **42**: 1323-1332 [PMID: 24705898 DOI: 10.1177/0363546514528864]
- 7 **Osborn DC**, Cain EL, Raines BT, Fortenbaugh D, Dugas JR, Andrews JR. Long-term Outcomes After Ulnar Collateral Ligament Reconstruction in Competitive Baseball Players: Minimum 10-Year Follow-up. *Am J Sports Med* 2014; **42**: 1333-1342 [PMID: 24705899 DOI: 10.1177/0363546514528870]
- 8 **Park JY**, Oh KS, Bahng SC, Chung SW, Choi JH. Does well maintained graft provide consistent return to play after medial ulnar collateral ligament reconstruction of the elbow joint in elite baseball players? *Clin Orthop Surg* 2014; **6**: 190-195 [PMID: 24900901 DOI: 10.4055/cios.2014.6.2.190]
- 9 **Rohrbough JT**, Altchek DW, Hyman J, Williams RJ, Botts JD. Medial collateral ligament reconstruction of the elbow using the docking technique. *Am J Sports Med* 2002; **30**: 541-548 [PMID: 12130409]
- 10 **Conway JE**, Jobe FW, Glousman RE, Pink M. Medial instability of the elbow in throwing athletes. Treatment by repair or reconstruction of the ulnar collateral ligament. *J Bone Joint Surg Am* 1992; **74**: 67-83 [PMID: 1734015]
- 11 **Dodson CC**, Thomas A, Dines JS, Nho SJ, Williams RJ, Altchek DW. Medial ulnar collateral ligament reconstruction of the elbow in throwing athletes. *Am J Sports Med* 2006; **34**: 1926-1932 [PMID: 16902233 DOI: 10.1177/0363546506290988]
- 12 **Fleisig GS**, Andrews JR, Cutter GR, Weber A, Loftice J, McMichael C, Hassell N, Lyman S. Risk of serious injury for young baseball pitchers: a 10-year prospective study. *Am J Sports Med* 2011; **39**: 253-257 [PMID: 21098816 DOI: 10.1177/0363546510384224]
- 13 **Olsen SJ**, Fleisig GS, Dun S, Loftice J, Andrews JR. Risk factors for shoulder and elbow injuries in adolescent baseball pitchers. *Am J Sports Med* 2006; **34**: 905-912 [PMID: 16452269 DOI: 10.1177/0363546505284188]
- 14 **Bernas GA**, Ruberte Thiele RA, Kinnaman KA, Hughes RE, Miller BS, Carpenter JE. Defining safe rehabilitation for ulnar collateral ligament reconstruction of the elbow: a biomechanical study. *Am J Sports Med* 2009; **37**: 2392-2400 [PMID: 19684292 DOI: 10.1177/0363546509340658]
- 15 **Ellenbecker TS**, Wilk KE, Altchek DW, Andrews JR. Current concepts in rehabilitation following ulnar collateral ligament reconstruction. *Sports Health* 2009; **1**: 301-313 [PMID: 23015887 DOI: 10.1177/1941738109338553]
- 16 **Rettig AC**, Sherrill C, Snead DS, Mandler JC, Mielsing P. Nonoperative treatment of ulnar collateral ligament injuries in throwing athletes. *Am J Sports Med* 2001; **29**: 15-17 [PMID: 11206249]
- 17 **Dines JS**. Platelet rich plasma can successfully treat elbow ulnar collateral ligament insufficiency in high-level throwers. *Amer J Orthp* 2016; **5**: 2016
- 18 **Podesta L**, Crow SA, Volkmer D, Bert T, Yocum LA. Treatment of partial ulnar collateral ligament tears in the elbow with platelet-rich plasma. *Am J Sports Med* 2013; **41**: 1689-1694 [PMID: 23666850 DOI: 10.1177/0363546513487979]
- 19 **Walsh WR**, Wiggins ME, Fadale PD, Ehrlich MG. Effects of a delayed steroid injection on ligament healing using a rabbit medial collateral ligament model. *Biomaterials* 1995; **16**: 905-910 [PMID: 8562778]
- 20 **Richard MJ**, Aldridge JM, Wiesler ER, Ruch DS. Traumatic valgus instability of the elbow: pathoanatomy and results of direct repair. *J Bone Joint Surg Am* 2008; **90**: 2416-2422 [PMID: 18978410 DOI: 10.2106/JBJS.G.01448]
- 21 **Savoie FH**, Trenhaile SW, Roberts J, Field LD, Ramsey JR. Primary repair of ulnar collateral ligament injuries of the elbow in young athletes: a case series of injuries to the proximal and distal ends of the ligament. *Am J Sports Med* 2008; **36**: 1066-1072 [PMID: 18443280 DOI: 10.1177/0363546508315201]
- 22 **Smith GR**, Altchek DW, Pagnani MJ, Keeley JR. A muscle-splitting approach to the ulnar collateral ligament of the elbow. Neuroanatomy and operative technique. *Am J Sports Med* 1996; **24**: 575-580 [PMID: 8883675]
- 23 **Dines JS**, Yocum LA, Frank JB, ElAttrache NS, Gambardella RA, Jobe FW. Revision surgery for failed elbow medial collateral ligament reconstruction. *Am J Sports Med* 2008; **36**: 1061-1065 [PMID: 18443277 DOI: 10.1177/0363546508314796]
- 24 **Jones KJ**, Conte S, Patterson N, ElAttrache NS, Dines JS. Functional outcomes following revision ulnar collateral ligament

- reconstruction in Major League Baseball pitchers. *J Shoulder Elbow Surg* 2013; **22**: 642-646 [PMID: 23590886 DOI: 10.1016/j.jse.2013.01.031]
- 25 **Marshall NE**, Keller RA, Lynch JR, Bey MJ, Moutzouros V. Pitching performance and longevity after revision ulnar collateral ligament reconstruction in Major League Baseball pitchers. *Am J Sports Med* 2015; **43**: 1051-1056 [PMID: 25862037 DOI: 10.1177/0363546515579636]
- 26 **Thompson WH**, Jobe FW, Yocum LA, Pink MM. Ulnar collateral ligament reconstruction in athletes: muscle-splitting approach without transposition of the ulnar nerve. *J Shoulder Elbow Surg* 2001; **10**: 152-157 [PMID: 11307079 DOI: 10.1067/mse.2001.112881]
- 27 **Cain EL**, Andrews JR, Dugas JR, Wilk KE, McMichael CS, Walter JC, Riley RS, Arthur ST. Outcome of ulnar collateral ligament reconstruction of the elbow in 1281 athletes: Results in 743 athletes with minimum 2-year follow-up. *Am J Sports Med* 2010; **38**: 2426-2434 [PMID: 20929932 DOI: 10.1177/0363546510378100]
- 28 **Paletta GA**, Wright RW. The modified docking procedure for elbow ulnar collateral ligament reconstruction: 2-year follow-up in elite throwers. *Am J Sports Med* 2006; **34**: 1594-1598 [PMID: 16832125 DOI: 10.1177/0363546506289884]
- 29 **Bowers AL**, Dines JS, Dines DM, Altchek DW. Elbow medial ulnar collateral ligament reconstruction: clinical relevance and the docking technique. *J Shoulder Elbow Surg* 2010; **19**: 110-117 [PMID: 20188276 DOI: 10.1016/j.jse.2010.01.005]
- 30 **Ahmad CS**, Lee TQ, ElAttrache NS. Biomechanical evaluation of a new ulnar collateral ligament reconstruction technique with interference screw fixation. *Am J Sports Med* 2003; **31**: 332-337 [PMID: 12750123]
- 31 **Dines JS**, ElAttrache NS, Conway JE, Smith W, Ahmad CS. Clinical outcomes of the DANE TJ technique to treat ulnar collateral ligament insufficiency of the elbow. *Am J Sports Med* 2007; **35**: 2039-2044 [PMID: 17703003 DOI: 10.1177/0363546507305802]
- 32 **Dargel J**, Küpper F, Wegmann K, Oppermann J, Eysel P, Müller LP. Graft diameter does not influence primary stability of ulnar collateral ligament reconstruction of the elbow. *J Orthop Sci* 2015; **20**: 307-313 [PMID: 25790750 DOI: 10.1007/s00776-014-0688-y]
- 33 **Muller B**, Bowman KF, Bedi A. ACL graft healing and biologics. *Clin Sports Med* 2013; **32**: 93-109 [PMID: 23177465 DOI: 10.1016/j.csm.2012.08.010]
- 34 **Nossov S**, Dines JS, Murrell GA, Rodeo SA, Bedi A. Biologic augmentation of tendon-to-bone healing: scaffolds, mechanical load, vitamin D, and diabetes. *Instr Course Lect* 2014; **63**: 451-462 [PMID: 24720330]
- 35 **Joshi SM**, Mastrangelo AN, Magarian EM, Fleming BC, Murray MM. Collagen-platelet composite enhances biomechanical and histologic healing of the porcine anterior cruciate ligament. *Am J Sports Med* 2009; **37**: 2401-2410 [PMID: 19940313 DOI: 10.1177/0363546509339915]
- 36 **Murray MM**, Spindler KP, Devin C, Snyder BS, Muller J, Takahashi M, Ballard P, Nannery LB, Zurakowski D. Use of a collagen-platelet rich plasma scaffold to stimulate healing of a central defect in the canine ACL. *J Orthop Res* 2006; **24**: 820-830 [PMID: 16555312 DOI: 10.1002/jor.20073]
- 37 **Bissell L**, Tibrewal S, Sahni V, Khan WS. Growth factors and platelet rich plasma in anterior cruciate ligament reconstruction. *Curr Stem Cell Res Ther* 2014; **10**: 19-25 [PMID: 25012741]
- 38 **Xie X**, Zhao S, Wu H, Xie G, Huangfu X, He Y, Zhao J. Platelet-rich plasma enhances autograft revascularization and reinnervation in a dog model of anterior cruciate ligament reconstruction. *J Surg Res* 2013; **183**: 214-222 [PMID: 23472861 DOI: 10.1016/j.jss.2013.01.020]
- 39 **Del Torto M**, Enea D, Panfoli N, Filardo G, Pace N, Chiusaroli M. Hamstrings anterior cruciate ligament reconstruction with and without platelet rich fibrin matrix. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3614-3622 [PMID: 25173508 DOI: 10.1007/s00167-014-3260-6]
- 40 **Valentí Azcárate A**, Lamo-Espinosa J, Aquerreta Beola JD, Hernandez Gonzalez M, Mora Gasque G, Valentí Nin JR. Comparison between two different platelet-rich plasma preparations and control applied during anterior cruciate ligament reconstruction. Is there any evidence to support their use? *Injury* 2014; **45** Suppl 4: S36-S41 [PMID: 25384473 DOI: 10.1016/S0020-1383(14)70008-7]
- 41 **Chang CH**, Chen CH, Liu HW, Whu SW, Chen SH, Tsai CL, Hsiue GH. Bioengineered periosteal progenitor cell sheets to enhance tendon-bone healing in a bone tunnel. *Biomed J* 2012; **35**: 473-480 [PMID: 23442360 DOI: 10.4103/2319-4170.104412]
- 42 **Lui PP**, Wong OT, Lee YW. Application of tendon-derived stem cell sheet for the promotion of graft healing in anterior cruciate ligament reconstruction. *Am J Sports Med* 2014; **42**: 681-689 [PMID: 24451112 DOI: 10.1177/0363546513517539]
- 43 **Kibler WB**, Press J, Sciascia A. The role of core stability in athletic function. *Sports Med* 2006; **36**: 189-198 [PMID: 16526831]
- 44 **Wilk KE**, Meister K, Andrews JR. Current concepts in the rehabilitation of the overhead throwing athlete. *Am J Sports Med* 2002; **30**: 136-151 [PMID: 11799012]
- 45 **Wilk KE**, Hooks TR, Macrina LC. The modified sleeper stretch and modified cross-body stretch to increase shoulder internal rotation range of motion in the overhead throwing athlete. *J Orthop Sports Phys Ther* 2013; **43**: 891-894 [PMID: 24175603 DOI: 10.2519/jospt.2013.4990]
- 46 **McClure P**, Balaicuis J, Heiland D, Broersma ME, Thorndike CK, Wood A. A randomized controlled comparison of stretching procedures for posterior shoulder tightness. *J Orthop Sports Phys Ther* 2007; **37**: 108-114 [PMID: 17416125 DOI: 10.2519/jospt.2007.2337]
- 47 **Kibler WB**, Uhl TL, Maddux JW, Brooks PV, Zeller B, McMullen J. Qualitative clinical evaluation of scapular dysfunction: a reliability study. *J Shoulder Elbow Surg* 2002; **11**: 550-556 [PMID: 12469078 DOI: 10.1067/mse.2002.126766]
- 48 **Smith J**, Dietrich CT, Kotajarvi BR, Kaufman KR. The effect of scapular protraction on isometric shoulder rotation strength in normal subjects. *J Shoulder Elbow Surg* 2006; **15**: 339-343 [PMID: 16679235 DOI: 10.1016/j.jse.2005.08.023]
- 49 **Ben Kibler BW**, Sciascia A. What went wrong and what to do about it: pitfalls in the treatment of shoulder impingement. *Instr Course Lect* 2008; **57**: 103-112 [PMID: 18399573]
- 50 **Wilk KE**, Ellenbecker TS, Macrina LC. Rehabilitation of the Overhead Athlete's Elbow, in Elbow Ulnar Collateral Ligament Injury. In: Dines JS, Altchek DW. Springer Science Business Media: New York, 2015: 227-259
- 51 **Fleisig GS**, Andrews JR, Dillman CJ, Escamilla RF. Kinetics of baseball pitching with implications about injury mechanisms. *Am J Sports Med* 1995; **23**: 233-239 [PMID: 7778711]
- 52 **Wilk KE**, Obma P, Simpson CD, Cain EL, Dugas JR, Andrews JR. Shoulder injuries in the overhead athlete. *J Orthop Sports Phys Ther* 2009; **39**: 38-54 [PMID: 19194026 DOI: 10.2519/jospt.2009.2929]
- 53 **Wilk KE**, Yenchak AJ, Arrigo CA, Andrews JR. The Advanced Throwers Ten Exercise Program: a new exercise series for enhanced dynamic shoulder control in the overhead throwing athlete. *Phys Sportsmed* 2011; **39**: 90-97 [PMID: 22293772 DOI: 10.3810/psm.2011.11.1943]
- 54 **Reinold MM**, Wilk KE, Reed J, Crenshaw K, Andrews JR. Interval sport programs: guidelines for baseball, tennis, and golf. *J Orthop Sports Phys Ther* 2002; **32**: 293-298 [PMID: 12061709 DOI: 10.2519/jospt.2002.32.6.293]
- 55 **O'Hagan T**, Stucken C, Dodson CC. Sports Specific Outcomes for Ulnar Collateral Ligament Reconstruction, in Elbow Ulnar Collateral Ligament Injury. In: Dines JS, Altchek DW. Springer Science Business Media: New York, 2015: 219-226
- 56 **Dodson CC**, Slenker N, Cohen SB, Ciccotti MG, DeLuca P. Ulnar collateral ligament injuries of the elbow in professional football quarterbacks. *J Shoulder Elbow Surg* 2010; **19**: 1276-1280 [PMID: 20609599 DOI: 10.1016/j.jse.2010.05.028]
- 57 **Kenter K**, Behr CT, Warren RF, O'Brien SJ, Barnes R. Acute elbow injuries in the National Football League. *J Shoulder Elbow Surg* 2000; **9**: 1-5 [PMID: 10717854]

58 **Argo D**, Trenhaile SW, Savoie FH, Field LD. Operative treatment of ulnar collateral ligament insufficiency of the elbow in female

athletes. *Am J Sports Med* 2006; **34**: 431-437 [PMID: 16282580
DOI: 10.1177/0363546505281240]

P- Reviewer: Erickson BJ, Seijas R **S- Editor:** Qiu S **L- Editor:** A
E- Editor: Wu HL



Sternoclavicular joint dislocation and its management: A review of the literature

Daniel J Morell, David S Thyagarajan

Daniel J Morell, David S Thyagarajan, Department of Trauma and Orthopaedic Surgery, Northern General Hospital, Sheffield Teaching Hospitals NHS Trust, Sheffield S5 7AU, United Kingdom

Author contributions: Morell DJ and Thyagarajan DS were involved in the literature search, writing and editing of this manuscript.

Conflict-of-interest statement: Authors declare no conflict of interests for this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dr. David S Thyagarajan, Consultant in Trauma and Orthopaedics, Department of Trauma and Orthopaedic Surgery, Northern General Hospital, Sheffield Teaching Hospitals NHS Trust, Sheffield S5 7AU, United Kingdom. davidskt@yahoo.co.uk
Telephone: +44-781-5785916

Received: May 28, 2015
Peer-review started: June 1, 2015
First decision: August 16, 2015
Revised: December 11, 2015
Accepted: January 5, 2016
Article in press: January 7, 2016
Published online: April 18, 2016

Abstract

Dislocations of the sternoclavicular joint (SCJ) occur with relative infrequency and can be classified into anterior and posterior dislocation, with the former being more common. The SCJ is inherently unstable due to its lack of articular contact and therefore relies on stability

from surrounding ligamentous structures, such as the costoclavicular, interclavicular and capsular ligaments. The posterior capsule has been shown in several studies to be the most important structure in determining stability irrespective of the direction of injury. Posterior dislocation of the SCJ can be associated with life threatening complications such as neurovascular, tracheal and oesophageal injuries. Due to the high mortality associated with such complications, these injuries need to be recognised acutely and managed promptly. Investigations such as X-ray imaging are poor at delineating anatomy at the level of the mediastinum and therefore CT imaging has become the investigation of choice. Due to its rarity, the current guidance on how to manage acute and chronic dislocations is debatable. This analysis of historical and recent literature aims to determine guidance on current thinking regarding SCJ instability, including the use of the Stanmore triangle. The described methods of reduction for both anterior and posterior dislocations and the various surgical reconstructive techniques are also discussed.

Key words: Sternoclavicular joint dislocation; Reduction; Reconstruction; Stabilisation; Surgery

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Most anterior sternoclavicular joint (SCJ) dislocations can be managed non-surgically. A small subgroup of these patients develop persistent symptomatic anterior instability. While most tolerate these symptoms well some find this disabling and surgical stabilisation in such cases have shown satisfactory results. Posterior SCJ dislocation can be subtle and needs prompt identification and immediate closed reduction but if unstable will require surgical stabilisation.

Morell DJ, Thyagarajan DS. Sternoclavicular joint dislocation and its management: A review of the literature. *World J Orthop*

2016; 7(4): 244-250 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/244.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.244>

INTRODUCTION

Sternoclavicular joint dislocations are rare and represent only 3% of all dislocations around the shoulder^[1]. Despite the uncommon nature of these injuries they can present the clinician with uncertainty regarding their investigation and management. Dislocations may be either traumatic or atraumatic. Those that are due to trauma may dislocate anteriorly or posteriorly, with anterior dislocation being approximately nine times more common. The main concern with a posterior dislocation is the risk of compression to the mediastinal structures which may be life threatening, requiring expedient intervention^[2]. Atraumatic dislocations and subluxations may occur in patients with collagen deficiency conditions such as generalised hypermobility syndrome and Ehlers-Danlos^[3,4], or clavicular deformity, abnormal muscle patterning, infection or arthritis. The purpose of this educational review is clarify the current thinking regarding the diagnosis of all types of sternoclavicular joint (SCJ) dislocation and how these challenging injuries can be managed^[5].

ANATOMY

The SCJ is the only bony articulation between the axial skeleton and the upper extremity^[6]. The clavicle is unique in the sense that it is the first bone in the human body to ossify, usually in the fifth gestational week but the medial end of the clavicle is the last to fuse, between ages 23-25^[7]. Therefore in some patients under 25, what is believed to be an SCJ dislocation is actually a fracture of medial clavicular physis and owing to the remodelling potential of such paediatric injuries can usually be managed conservatively^[8].

The SCJ is a diarthrodial saddle type synovial joint which is inherently unstable^[8,9]. Less than 50% of the medial clavicular surface articulates with its corresponding articular surface on the manubrium sterni. Its stability is therefore derived from intrinsic and extrinsic ligamentous structures surrounding the joint^[8]. These structures include the costoclavicular (rhomboid) ligament, which is divided into an anterior and posterior fasciculus. The anterior fasciculus resists superior rotation and lateral displacement and the posterior fasciculus resists inferior rotation and medial displacement. The interclavicular ligament (extrinsic) and the posterior and anterior sternoclavicular ligaments also aid stability along with the anterior and posterior capsular ligaments. In 1967, Bearn^[10] conducted an anatomical study looking at the structures which were of paramount importance in maintaining SCJ stability. By dividing all the ligamentous structures

except the capsular restraints there was found to be no effect on the position of the clavicle. However dividing the capsular ligaments in isolation resulted in a superior migration of the medial clavicle. This work was repeated by Spencer *et al*^[6] in 2002 and showed that the posterior capsule is the joints strongest ligamentous stabiliser. Sectioning of the posterior capsule resulted in 41% increase in anterior translation and a 106% increase in posterior translation. When the anterior capsule was cut in isolation this resulted in just a 25% increase in anterior translation and 0.7% increase in posterior translation. Therefore in reconstructive surgery close attention should be paid to the posterior capsule whether the dislocation is anterior or posterior^[6].

The SCJ contains a fibrocartilaginous disc which is attached to the anterior and posterior sternoclavicular ligaments and capsule, dividing the SCJ into two synovium-lined cavities^[8]. This disc degenerates with time and by the patients 70's or 80's is incomplete^[11]. Tears of this disc can be a cause of pain in the younger patient.

Subclavius arises from the first rib just lateral to the costoclavicular ligament and inserts onto the inferior surface of the clavicle. It is believed to have a protective function with regards to the stability of the SCJ by reducing the rate of upward displacement of the clavicle when it is under lateral compressive loads^[8].

BIOMECHANICS

Any movement at the shoulder girdle results in some degree of movement at the SCJ. The clavicle elevates about 4 degrees for every 10 degrees of arm forward flexion^[12]. When the shoulders are retracted the SCJ translates anteriorly and the reverse for shoulder protraction. With combined movements the clavicle can rotate up to 40 degrees along its longitudinal axis. Patients with a short clavicle can result in significantly more torque at the SCJ^[8].

Posterior dislocation of the SCJ can be caused by a direct force over the anteromedial aspect of the clavicle or an indirect force to the posterolateral shoulder, forcing the medial clavicle posteriorly. Anterior dislocation is usually due to a lateral compressive force to the shoulder girdle, which results in sparing of the posterior capsule but rupture of the anterior capsule and often part of the costoclavicular ligament. As with all high energy injuries one should have a high index of suspicion for associated injuries^[8].

CLINICAL PRESENTATION

Patients presenting with these injuries are often in high energy collisions, whether that be sporting or through a motor vehicle accident^[13]. Those with anterior dislocations of the SCJ will complain of a painful lump just lateral to the sternum. Care needs to be taken to determine whether this is indeed a true dislocation or a fracture of the medial clavicle. As mentioned previously,



Figure 1 Serendipity view.

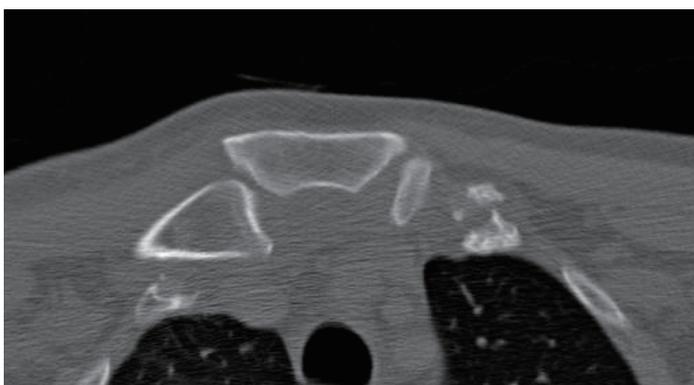


Figure 2 Computed tomography scan showing dislocation of the sternoclavicular joint.

if the patient is under 25 then consideration of the possibility of this being a physeal injury should be undertaken^[9].

Posterior dislocations present with medial clavicular pain but also may present with compressive symptoms such as dyspnoea or dysphagia or with vascular and neurological compromise. If any of these symptoms are present then urgent reduction is necessary. Patients often have the affected upper limb adducted across their chest to prevent excess glenohumeral or scapulothoracic movements. There will often be minimal swelling but may be some bruising below the medial aspect of the clavicle^[8].

On examination patients will have evidence of swelling and reduced upper limb range of movement. They may also present with new onset paraesthesia in the upper limb and/or weakened pulses or signs of venous congestion.

INVESTIGATIONS

Dislocations of the SCJ are notoriously difficult to visualise on plain radiographs. Routine chest radiographs have a poor sensitivity for picking up dislocations, however they mandatory if there is a suspicion of a posterior dislocation so as to rule out a pneumothorax, pneumomediastinum or haemopneumothorax^[8]. In 1975, Rockwood^[14] described the "serendipity" view (Figure 1) or 40 degree cephalic tilt which presents the anterior dislocation as a superiorly displaced medial clavicle and the posterior dislocation as an inferiorly displaced medial clavicle. Alternative views include

the Heinig view, in which the X-ray beam is directly perpendicular to the SCJ but with an oblique projection in the supine patient^[15]. This allows the SCJ to be visualised without underlying vertebral bodies distorting the view.

CT imaging is readily available 24 h a day in most trauma units and this is the investigation of choice (Figure 2). It has superior image resolution and allows 3D reconstruction of the SCJ to determine its exact position^[16] (Figure 3). MRI has a poorer resolution than CT but can be used to assess ligamentous injury and the condition of the other soft tissues posterior to the SCJ^[8].

If there is a suspicion of an intimal tear to the subclavian artery then CT angiography may be necessary.

CLASSIFICATION

Dislocations of the SCJ can be broadly classified by the direction of displacement, which may be anterior or posterior, superior or inferior. Dislocation of the SCJ is often not an isolated event and may be due to other structural causes than trauma. It can therefore be thought of as instability, which can be acute, recurrent or persistent. The Stanmore triangle, which is commonly used for glenohumeral instability, has also been applied to instability of the SCJ. The triangle consists of 3 polar groups; type I traumatic structural, type II atraumatic structural and type III muscle patterning, non structural. Patients may move around this triangle with time, for example a patient may initially present with a clear

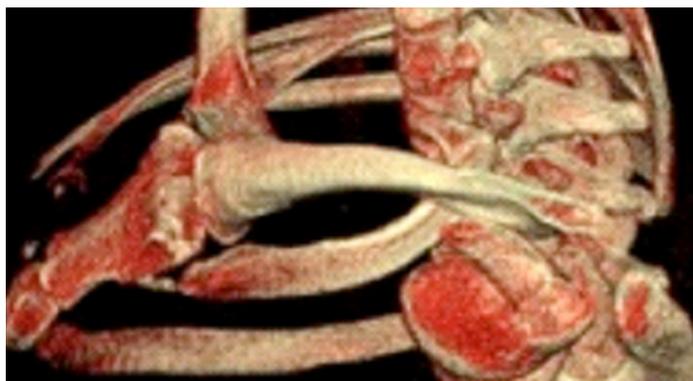


Figure 3 Computed tomography reconstruction of the sternoclavicular joint dislocation.

traumatic event but then as a result of abnormal movement due to pain may develop abnormal muscle patterning^[6].

With type I instability there is a clear history of trauma, whether this is a fracture of the medial clavicle or SCJ dislocation. With Type II there is no history of trauma but structural change within the capsular tissue, which may be as a result of repetitive microtrauma. In type III there is no structural abnormality and it is the abnormal contraction of muscles, namely pectoralis major, which cause the SCJ to sublux or dislocate^[6].

MANAGEMENT

Reduction of anterior dislocation

If the patient presents with an acute anterior dislocation of their SCJ (within 7-10 d) then these can be reduced by closed reduction with sedation or under general anaesthetic in the operating room. The patient is placed supine with a bolster placed between their shoulders. Traction is then applied to the affected upper limb in 90 degrees of abduction with neutral flexion and direct pressure is applied over the medial clavicle. Following reduction the arm should be placed in a polysling, maintaining scapular protraction for up to 4 wk. Redislocation has found to range between 21% and 100%^[17-19] which raises the question whether simple closed reduction without ligament reconstruction is sufficient. One can also question whether reduction of an anterior dislocation is necessary at all.

Bicos *et al*^[20] argues that anterior SCJ instability should primarily be treated conservatively. The patients should be informed there is a high risk of persistent instability with non-operative treatment, but this persistent instability will be well tolerated and have little functional impact in the vast majority. Most anterior SCJ instability can be managed without surgery. However a small sub group of these patients go on to develop persistent symptomatic instability requiring surgical stabilisation.

Reduction of posterior dislocation

Although these injuries are rare, complications such as oesophageal, tracheal or neurovascular injury occur in approximately 30% with a mortality rate of 3%-4%^[18].

Closed reduction under sedation should be attempted in patients presenting in the acute phase (within 7-10 d). Rockwood^[14] described a technique of reduction in which a towel clip is used percutaneously to grasp the medial clavicle and pull it anteriorly.

An alternative reduction tool is the abduction traction technique. The shoulder is abducted to 90 degrees and traction applied. An extension force is then applied to the shoulder resulting in anterior translation of the medial clavicle back into joint^[21].

In 1984 Buckerfield *et al*^[22] suggested a technique involving retraction of the shoulders with caudal traction on the adducted arm, while the patient is supported by an interscapular bolster. This achieved reduction in 6 out of 7 patients who had failed reduction through other means.

Open reduction and stabilisation

If closed reduction is not possible or there is on going symptomatic instability of the SCJ, there are numerous surgical techniques that have been described in the literature and there is no evidence that one method is superior over the other. Martínez *et al*^[23] describe a technique used in 1 posterior dislocation using gracilis tendon passed in a figure of 8 through drill holes in the manubrium and clavicle. At 1 year follow-up there was evidence of SCJ subluxation and erosion of both the manubrium and medial clavicle. Despite this patient was asymptomatic.

Booth *et al*^[24] reported a more successful technique in 5 SCJ's. The sternal origin of the sternocleidomastoid (SCM) with a strip of periosteum is detached and passed under the first rib and back through a drill hole in the clavicle and then tied back onto itself. In this way it has effectively reconstructed the costoclavicular ligament. No complications or failures were noted in this group.

Bae *et al*^[25] presented 15 cases in which either semitendinosus or SCM graft was passed through the medial clavicle and manubrium in a figure of 8. The medial 2-2.5 cm of clavicle was then resected. Results were mixed with 87% of patients achieving stability but 40% of patients complained of persistent pain.

More recently, Abiddin *et al*^[26] had success with the use of suture anchors, avoiding the need for graft.



Figure 4 Surgilig lockdown device.



Figure 5 Intraoperative picture of sternoclavicular joint stabilisation using surgilig lockdown.

Sutures were placed through drill holes in the medial clavicle and manubrium combined with a capsular repair. He reported 2 failures, one of which was traumatic.

Franck *et al.*^[27] reported excellent results with the use of a Balsaer plate. The hook of this was inserted under the manubrium with the lateral aspect of the plate lying on the medial clavicle. No re-dislocations were reported in any of the 9 patients however metalwork needed to be removed a secondary procedure to prevent migration.

Wallace *et al.*^[28] reported their new technique of stabilising the SC joint by reconstructing the costoclavicular ligament using a braided polyester mesh device (Surgilig Lockdown) (Figures 4 and 5). In a separate study they had looked at the histological response of the braided polyester mesh device retrieved from AC joint and found outer capsule formation composed of collagen with fibroblast. This technique recreates the costoclavicular ligament and also stabilises the anterior and the posterior capsule during stabilisation. Their results showed no major or life threatening complication and all patients achieved good functional outcome and patient satisfaction^[28-30].

An important lesson was learned through the work of Lyons *et al.*^[31]. Rather than a soft tissue procedure they described the use of smooth and threaded k wires to stabilise 21 anterior SCJ dislocations. The results were catastrophic with 8 deaths due to wire migration into major vascular structures. A further 6 patients only survived cardiac tamponade following surgical intervention. In later work Rockwood *et al.*^[32] described excision arthroplasty of the medial 1.5 cm of the clavicle. However, he found that in those with a ruptured CCL requiring reconstruction then excision of the medial clavicle was unsatisfactory.

In patients with type II instability of the SCJ, the usual presentation is prominence of the medial clavicle and pain felt on overhead activities. There is often a history of generalised ligamentous laxity. This group of patients can usually be managed with steroid injections and physiotherapy alone. Rockwood *et al.*^[33] looked at patients with atraumatic anterior dislocations and found that when treated conservatively 78% of patients had no restriction of lifestyle or activity, however 90% had persistent subluxation and 21% of these had

ongoing pain. Patients treated surgically all showed unsatisfactory results. Atraumatic posterior dislocations should be treated in a similar way to traumatic dislocations with open reduction and stabilisation due to the risk of compression to retrosternal structures.

Surgery is rarely indicated in type III instability of the SCJ. The problem is non-structural and due to abnormal muscle patterning. They may be investigated using EMG's to identify if the pectoralis major is being recruited inappropriately. Management is therefore with biofeedback physiotherapy which requires patient compliance and the re-learning of appropriate muscle contraction and proprioception^[34]. Surgery should be reserved for those patients who demonstrate some structural abnormality which has then gone on to develop abnormal muscle patterning (type II/III)^[8].

COMPLICATIONS

The main recognised complications are associated with traumatic posterior dislocations of the SCJ. Symptoms of compression of retrosternal structures have been reported to occur in up to a third of cases with life threatening consequences^[35]. Complications include brachial plexus and vascular injuries, oesophageal ruptures and tracheal compression and there have been 5 known reported cases of deaths^[2].

Untreated anterior dislocations will result in a longstanding cosmetic deformity, which some patients may find unsightly. Persistent pain and instability are the main reasons for failure of surgical stabilisation of SCJ injuries^[8].

THE FLOATING CLAVICLE

Dislocation of SCJ does not always occur in isolation and may occur in combination with the ACJ. This is known as bipolar clavicular dislocation or the traumatic floating clavicle. Only 40 cases have been described in the literature making this injury rare^[13]. The first case was described by Porral^[36] in 1831 and since then there has been intermittent reports of this injury, which in the majority of cases is due to high velocity road traffic

collisions, falls from height and heavy objects falling onto the shoulder. Management of this injury should be designed on an individual patient basis. All reported an anterior dislocation of the SCJ and posterior dislocation of the ACJ.

More recently the first ever-case report of floating clavicle with a unique combination of posterior SCJ dislocation with Grade III ACJ dislocation was reported. The authors had recommended surgical stabilisation of both SCJ and the ACJ for this injury^[37].

CONCLUSION

Dislocations of the SCJ are rare and may result from direct trauma as an acute occurrence or in the more persistent case of atraumatic structural instability or non structural abnormal muscle patterning. Traumatic structural dislocation should be investigated appropriately with the use of CT if the diagnosis is unclear. The use of acute reduction of anterior dislocations is debatable as up to 100% re-dislocate and reduction techniques are not without risk. Posterior dislocations with compressive symptoms need to be reduced promptly to prevent life threatening complications. Persistent pain and instability can be managed surgically through a variety of means. Surgical stabilisation using braided polyester weave device (Surgilig Lockdown) has shown promising results in the functional outcome studies that I have been involved in. The use of pin transfixation however is absolutely contraindicated due to the high risk of pin migration and death.

Surgical management of SCJ injuries are technically demanding. The surgeon should be familiar with the complex anatomy and it is recommended that these procedures be carried out in large centres with cardiothoracic surgical back up if required to deal with any intra operative or post operative complications.

REFERENCES

- 1 **Cave E.** Shoulder girdle injuries. In: Fractures and other injuries. Chicago: Year book publishers, 1958: 58-259
- 2 **Garg S, Alshameeri ZA, Wallace WA.** Posterior sternoclavicular joint dislocation in a child: a case report with review of literature. *J Shoulder Elbow Surg* 2012; **21**: e11-e16 [PMID: 22005127 DOI: 10.1016/j.jse.2011.07.007]
- 3 **Iglesias JL, Renard T.** Diaphragmatic hernia in an 8-year-old with Ehlers-Danlos syndrome. *Pediatr Surg Int* 1998; **13**: 553-555 [PMID: 9799373 DOI: 10.1007/s003830050401]
- 4 **Finsterbush A, Pogrand H.** The hypermobility syndrome. Musculoskeletal complaints in 100 consecutive cases of generalized joint hypermobility. *Clin Orthop Relat Res* 1982; **(168)**: 124-127 [PMID: 7105534 DOI: 10.1097/00003086-198208000-00024]
- 5 **Medvecky MJ, Zuckerman JD.** Sternoclavicular joint injuries and disorders. *Instr Course Lect* 2000; **49**: 397-406 [PMID: 10829191]
- 6 **Spencer EE, Kuhn JE, Huston LJ, Carpenter JE, Hughes RE.** Ligamentous restraints to anterior and posterior translation of the sternoclavicular joint. *J Shoulder Elbow Surg* 2002; **11**: 43-47 [PMID: 11845148 DOI: 10.1067/mse.2002.119394]
- 7 **Wirth MA, Rockwood CA.** Acute and Chronic Traumatic Injuries of the Sternoclavicular Joint. *J Am Acad Orthop Surg* 1996; **4**: 268-278 [PMID: 10797194]
- 8 **Sewell MD, Al-Hadithy N, Le Leu A, Lambert SM.** Instability of the sternoclavicular joint: current concepts in classification, treatment and outcomes. *Bone Joint J* 2013; **95-B**: 721-731 [PMID: 23723264 DOI: 10.1302/0301-620X.95B6.31064]
- 9 **Tepolt F, Carry PM, Heyn PC, Miller NH.** Posterior sternoclavicular joint injuries in the adolescent population: a meta-analysis. *Am J Sports Med* 2014; **42**: 2517-2524 [PMID: 24569702 DOI: 10.1177/0363546514523386]
- 10 **Bearn JG.** Direct observations on the function of the capsule of the sternoclavicular joint in clavicular support. *J Anat* 1967; **101**: 159-170 [PMID: 6047697]
- 11 **van Tongel A, MacDonald P, Leiter J, Pouliart N, Peeler J.** A cadaveric study of the structural anatomy of the sternoclavicular joint. *Clin Anat* 2012; **25**: 903-910 [PMID: 22991168 DOI: 10.1002/ca.22021]
- 12 **Inman VT, Saunders JB, Abbott LC.** Observations of the function of the shoulder joint. 1944. *Clin Orthop Relat Res* 1996; **(330)**: 3-12 [PMID: 8804269 DOI: 10.1097/00003086-199609000-00002]
- 13 **Choo C, Wong H, Nordin A.** Traumatic floating clavicle: a case report. *Malays Orthop J* 2012; **6**: 57-59 [PMID: 25279061 DOI: 10.5704/MOJ.1207.008]
- 14 **Rockwood CA.** Dislocations of the sternoclavicular joint. In: Evans E. American academy of orthopaedic surgeons instructional course lectures: Volume XXIV. St. Louis: CV Mosby, 1975: 144-159
- 15 **Robinson CM, Jenkins PJ, Markham PE, Beggs I.** Disorders of the sternoclavicular joint. *J Bone Joint Surg Br* 2008; **90**: 685-696 [PMID: 18539660 DOI: 10.1302/0301-620X.90B6.20391]
- 16 **Levinsohn EM, Bunnell WP, Yuan HA.** Computed tomography in the diagnosis of dislocations of the sternoclavicular joint. *Clin Orthop Relat Res* 1979; **(140)**: 12-16 [PMID: 477062 DOI: 10.1097/00003086-197905000-00002]
- 17 **Savastano AA, Stutz SJ.** Traumatic sternoclavicular dislocation. *Int Surg* 1978; **63**: 10-13 [PMID: 627448]
- 18 **Nettles JL, Linscheid RL.** Sternoclavicular dislocations. *J Trauma* 1968; **8**: 158-164 [PMID: 5645243 DOI: 10.1097/00005373-196803000-00004]
- 19 **Eskola A.** Sternoclavicular dislocation. A plea for open treatment. *Acta Orthop Scand* 1986; **57**: 227-228 [PMID: 3739662 DOI: 10.3109/17453678608994382]
- 20 **Bicos J, Nicholson GP.** Treatment and results of sternoclavicular joint injuries. *Clin Sports Med* 2003; **22**: 359-370 [PMID: 12825536 DOI: 10.1016/S0278-5919(02)00112-6]
- 21 **Rockwood CA, Wirth M.** Injuries to the sternoclavicular joint. In: Rockwood CA, Green D, Buchholz R, Heckman J. Rockwood and Green's fractures in adults. Philadelphia: 1996: 1415-1471
- 22 **Buckerfield CT, Castle ME.** Acute traumatic retrosternal dislocation of the clavicle. *J Bone Joint Surg Am* 1984; **66**: 379-385 [PMID: 6699054]
- 23 **Martínez A, Rodríguez A, González G, Herrera A, Domingo J.** Atraumatic spontaneous posterior subluxation of the sternoclavicular joint. *Arch Orthop Trauma Surg* 1999; **119**: 344-346 [PMID: 10447637 DOI: 10.1007/s004020050424]
- 24 **Booth CM, Roper BA.** Chronic dislocation of the sternoclavicular joint: an operative repair. *Clin Orthop Relat Res* 1979; **(140)**: 17-20 [PMID: 477070 DOI: 10.1097/00003086-197905000-00003]
- 25 **Bae DS, Kocher MS, Waters PM, Micheli LM, Griffey M, Dichtel L.** Chronic recurrent anterior sternoclavicular joint instability: results of surgical management. *J Pediatr Orthop* 2006; **26**: 71-74 [PMID: 16439906 DOI: 10.1097/01.bpo.0000187998.91837.b2]
- 26 **Abiddin Z, Sinopidis C, Grocock CJ, Yin Q, Frostick SP.** Suture anchors for treatment of sternoclavicular joint instability. *J Shoulder Elbow Surg* 2006; **15**: 315-318 [PMID: 16679231 DOI: 10.1016/j.jse.2005.07.005]
- 27 **Franck WM, Jannasch O, Siassi M, Hennig FF.** Balsaer plate stabilization: an alternate therapy for traumatic sternoclavicular instability. *J Shoulder Elbow Surg* 2003; **12**: 276-281 [PMID: 12851582 DOI: 10.1016/S1058-2746(02)86802-1]
- 28 **Wallace WA, Thyagarajan D.** Open Reduction and Stabilisation of a Locked Posterior Dislocation of the Sterno-Clavicular Joint with LockDown™ 34th SICOT Orthopaedic World Congress, October 2013, Hyderabad, India. Available from: URL: <http://www.sicot.org>

- org/.../Final%20Programme%20-%20Hyderabad%20-%20we
- 29 **Kocsis G**, McCulloch TA, Thyagarajan D, Wallace WA. The biological response to a failed extra-articular polyester ligament used for AC Joint reconstruction at the shoulder girdle: a retrieval analysis of five cases. *Bone Joint J* 2015; **97-B**: 83-88 [PMID: 25568418 DOI: 10.1302/0301-620X.97B1.34357]
- 30 **Thyagarajan D**, Kocsis G, Wallace WA. Surgical stabilisation for sternoclavicular joint instability (Unpublised) SECEC congress 17-20 September 2014, Istanbul. Available from: URL: http://www.secec2015.com/wp.../2014/06/SECEC_2014_Congress_Program
- 31 **Lyons FA**, Rockwood CA. Migration of pins used in operations on the shoulder. *J Bone Joint Surg Am* 1990; **72**: 1262-1267 [PMID: 2204634]
- 32 **Rockwood CA**, Groh GI, Wirth MA, Grassi FA. Resection arthroplasty of the sternoclavicular joint. *J Bone Joint Surg Am* 1997; **79**: 387-393 [PMID: 9070528]
- 33 **Rockwood CA**, Odor JM. Spontaneous atraumatic anterior subluxation of the sternoclavicular joint. *J Bone Joint Surg Am* 1989; **71**: 1280-1288 [PMID: 2793879]
- 34 **Jaggi A**, Lambert S. Rehabilitation for shoulder instability. *Br J Sports Med* 2010; **44**: 333-340 [PMID: 20371558 DOI: 10.1136/bjism.2009.059311]
- 35 **Ono K**, Inagawa H, Kiyota K, Terada T, Suzuki S, Maekawa K. Posterior dislocation of the sternoclavicular joint with obstruction of the innominate vein: case report. *J Trauma* 1998; **44**: 381-383 [PMID: 9498516 DOI: 10.1097/00005373-199802000-00027]
- 36 **Porral A**. Observation of a double dislocation of the right clavicle. *J Univ Hebd Chir Prat* 1831; **2**: 78-82
- 37 **Thyagarajan D**, Webb M, Wallace WA. A rare case of floating clavicle and a novel technique for stabilizing the sternoclavicular joint. *Shoulder & Elbow* 2015; **7**: 44-48 [DOI: 10.1177/1758573214536534]

P- Reviewer: Emara K, Hernandez-Sanchez S, Yamakado K
S- Editor: Gong ZM **L- Editor:** A **E- Editor:** Wu HL



Retrospective Cohort Study

Promising short-term clinical results of the cementless Oxford phase III medial unicondylar knee prosthesis

Karin B van Dorp, Stefan JM Breugem, Daniël J Bruijn, Marcel JM Driessen

Karin B van Dorp, Stefan JM Breugem, Daniël J Bruijn, Marcel JM Driessen, Orthopedium Clinics, 2616 LS Delft, Zuid-Holland, the Netherland

Author contributions: All the authors contributed equally to this paper.

Institutional review board statement: The study was reviewed and approved by the medical research ethics board of Rotterdam.

Informed consent statement: All study participants provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All the authors declare not to have a conflict of interest related to the manuscript.

Data sharing statement: All study participants agreed with anonymous data sharing. The original anonymous dataset is available on request from the corresponding author.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Karin B van Dorp, MD, Orthopedium Clinics, Olof Palmerstraat 20, 2616 LS Delft, Zuid-Holland, the Netherland. k.b.vandorp@gmail.com
Telephone: +31-8-80088444
Fax: +31-8-80088445

Received: May 29, 2015

Peer-review started: June 1, 2015

First decision: August 25, 2015

Revised: December 17, 2015

Accepted: January 8, 2016

Article in press: January 11, 2016

Published online: April 18, 2016

Abstract

AIM: To investigate the short-term clinical results of the Oxford phase III cementless medial unicondylar knee prosthesis (UKP) compared to the cemented medial UKP.

METHODS: We conducted a cross-sectional study in a tertiary orthopedic centre between the period of May 2010 and September 2012. We included 99 medial UKP in 97 patients and of these UKP, 53 were cemented and 46 were cementless. Clinical outcome was measured using a questionnaire, containing a visual analogue scale (VAS) for pain, Oxford Knee score, Kujala score and SF-12 score. Knee function was tested using the American Knee Society score. Complications, reoperations and revisions were recorded. Statistical significance was defined as a P value < 0.05 .

RESULTS: In a mean follow-up time of 19.5 mo, three cemented medial UKP were revised to a total knee prosthesis. Reasons for revision were malrotation of the tibial component, aseptic loosening of the tibial component and progression of osteoarthritis in the lateral- and patellofemoral compartment. In five patients a successful reoperation was performed, because of impingement or (sub)luxation of the polyethylene bearing. Patients with a reoperation were significant younger than patients in the primary group (56.7 vs 64.0, $P = 0.01$) and were more likely to be male (85.7% vs 38.8%, $P = 0.015$). Overall the cementless medial UKP seems to perform better, but the differences in clinical outcome are not significant; a VAS pain score of 7.4 vs 11.7 ($P = 0.22$), an Oxford Knee score of 43.3 vs 41.7 ($P = 0.27$) and a Kujala score of 79.6 vs 78.0 ($P = 0.63$). The American Knee Society scores were slightly better in the cementless group with 94.5 vs 90.2 ($P = 0.055$) for the objective score and 91.2 vs 87.8 ($P = 0.25$) for the subjective score.

CONCLUSION: The cementless Oxford phase III medial UKP shows good short-term clinical results, when used in a specialist clinic by an experienced surgeon.

Key words: Knee osteoarthritis; Unicondylar knee arthroplasty; Cementless; Treatment outcome; Reoperation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The higher revision rate in unicondylar knee arthroplasty compared to total knee arthroplasty is a concern. The cementless unicondylar knee prosthesis (UKP) eliminates one of the technical errors related to failure; the cementing technique. The cementless Oxford UKP also shows reduced radiolucent lines at one year follow-up, whereas the cemented UKP shows occurrence of radiolucent lines. The developing hospital has published encouraging results of the cementless Oxford phase III medial UKP. In our independent retrospective cohort study we observed three revisions of cemented UKP. There were five successful reoperations. The cementless UKP seems to perform better, but no significant difference could be found.

van Dorp KB, Breugem SJM, Bruijn DJ, Driessen MJM. Promising short-term clinical results of the cementless Oxford phase III medial unicondylar knee prosthesis. *World J Orthop* 2016; 7(4): 251-257 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/251.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.251>

INTRODUCTION

The unicondylar knee prosthesis (UKP) is an established treatment for end-stage medial osteoarthritis (OA) of the knee and accounts for around 8%-10% of all primary knee replacements^[1,2]. One of the successful implants used, is the cemented Oxford medial UKP phase III. This is a fully congruent mobile bearing prosthesis, which is implanted *via* a minimal invasive procedure with minimal bone-loss. Success of the medial UKP is still largely related to the indication for UKP and the experience of the surgeon and the surgical team. This is confirmed by the lower survival rates of UKP in national registers compared to the survival rates of UKP implanted by specialized surgeons who perform UKP surgery regularly^[1,2].

The higher revision rates in unicondylar arthroplasty are a concern. The difference in revision rate between UKP and total knee prosthesis (TKP) is likely to be multi-factorial. A major issue seems to be the ease to choose for revision of a UKP compared to a revision of a TKP. With the introduction of the cementless Oxford UKP (2003) one of the technical errors related to failure, the cementing technique, can be eliminated.

Also, the cementless Oxford medial UKP shows reduced radiolucent lines at one year follow-up, whereas the cemented Oxford medial UKP shows occurrence of radiolucent lines during follow-up^[3]. The occurrence of these radiolucent lines is thought to be a misleading factor for revision in patients with unexplained pain after cemented UKP. The developing hospital has published encouraging results of the cementless Oxford phase III UKP^[3], as well as cementless UKP by other manufacturers^[4-6].

Since May 2010 the cementless Oxford phase III medial UKP is frequently used in our clinic besides the cemented Oxford phase III medial UKP. In accordance with earlier published results, it is our experience that the cementless Oxford UKP performs as well as, or even better than the cemented Oxford UKP. With this retrospective study we want to compare the short-term clinical outcome of the cemented and the cementless Oxford phase III medial UKP performed in an independent center by one single surgeon.

MATERIALS AND METHODS

Population

We conducted a cross-sectional study in an orthopedic center, specialized in prosthesiology and sports medicine. Between May 19, 2010 and September 01, 2011 a total of 106 medial UKP were implanted in 103 patients with primary medial osteoarthritis. For inclusion, patients had to meet the Oxford selection criteria for UKP and had to have a minimum follow-up of one year. Age, activity status and former high tibial osteotomy were not considered contra-indications. Exclusion criteria were patients who had surgery on their lower extremities less than 6 mo ago, hybrid fixation, patients with insufficient comprehension of the Dutch language and patients living abroad.

Of the 103 eligible patients, two patients were deceased at the time of follow-up and one patient refused participation. Four patients did not meet the inclusion criteria and were excluded from the study. Reasons for exclusion were: living abroad (two cemented UKP), surgery on the lower extremities less than 6 mo ago and Multiple Sclerosis with progressive muscle weakness (cementless UKP). In total 99 UKP in 97 patients were included in the study. All study participants provided informed written consent prior to study enrollment. All study participants agreed with anonymous data sharing.

Technique

The medial Oxford phase III cemented and the cementless UKP are similar in design, except for the cylindrical main peg and a smaller anterior peg added posterior to the main peg in the cementless femoral component. Additionally, the cementless UKP has a hydroxyapatite coating with a porous titanium under-coating to stimulate bone adhesion.

Table 1 Patient characteristics

	Cemented <i>n</i> = 53	Cementless <i>n</i> = 46	<i>P</i> value
Age (yr)	64.6 ± 8.2	62.2 ± 6.7	0.12
Sex			0.471
Male	21 (39.6%)	21 (45.7%)	
Female	32 (60.4%)	25 (54.3%)	
ASA			0.497
1	15 (28.3%)	10 (21.7%)	
2	30 (56.6%)	31 (67.4%)	
3	8 (15.1%)	5 (10.9%)	
BMI (kg/m ²)	27.7 ± 4.1	29.0 ± 4.7	0.17
Follow-up (mo)	20.5 ± 3.9	18.3 ± 4.5	0.02
Ahlbäck grade medial joint space			0.442
0 (> 3 mm)	0 (0%)	1 (2.2%)	
1 (< 3 mm)	41 (77.4%)	33 (71.7%)	
2 (Obliteration)	10 (18.9%)	12 (26.1%)	
3 (Attrition < 5 mm)	2 (3.8%)	0	
Ahlbäck grade lateral joint space			0.129
0 (> 3 mm)	53 (100%)	45 (95.7%)	
1 (< 3 mm)	0	2 (4.3%)	
2 (Obliteration)	0	0	
3 (Attrition < 5 mm)	0	0	
Ahlbäck grade patellofemoral joint space			0.139
0 (> 3 mm)	29 (54.7%)	18 (39.1%)	
1 (< 3 mm)	23 (43.4%)	28 (60.9%)	
2 (Obliteration)	1 (1.9%)	0	
3 (Attrition < 5 mm)	0	0	

BMI: Body mass index.

All surgeries were performed by the senior author (MD), who performs more than 100 UKP per year. A short medial arthrotomy was used, followed by a thorough inspection of the knee to make the final decision. If the chondropathy was limited to the antero-medial tibia plateau, the lateral compartment had full thickness cartilage in the weight-bearing areas and the ligaments were intact, the knee was fit for an UKP. A tourniquet was used in all cases. The surgical technique was performed as described in the Oxford operative manual, but without intramedullary alignment of the femur component, as we believe this enlarges the risk of haemarthrosis.

Patients were told to start active knee flexion and extension as soon as possible. Post-operative pain management consisted of Acetaminophen, Diclofenac and an epidural patient controlled pain pump with Chirocaïn/Sufentanil in the first ± 24 h. Full weight-bearing with two elbow crutches was started the second post-operative day. Thrombosis prophylaxis consisted of Nadroparine and a compression stocking for a period of 6 wk. Patients who did not reach full extension or had trouble reaching 90 degrees flexion at discharge started with physical therapy immediately. All other patient started physical therapy 2 wk post-operative, to ensure adequate wound healing the first two weeks.

Clinical and radiological evaluation

Except for patients who had a revision and patients who had a reoperation less than 6 mo ago, all patients received a questionnaire consisting a visual analogue

scale (VAS) for pain ranging from 0-100 (0 being no pain), the Oxford Knee score (OKS) scored from 48 to 0 with 48 being the best possible outcome^[7], the Kujala anterior knee pain score scored from 100 to 0 with 100 being the best possible score^[8] and the SF-12 health survey^[9]. If questions were left blank we contacted patients by phone. For clinical outcome we used the American Knee Society score^[10] (AKSS objective and subjective score both ranging from 0-100, with 100 being the best possible score) performed by the first author (Karin B van Dorp) or by one of the co-authors. Range of motion and alignment were measured with the patient in supine position and with a goniometer measuring in 5 degree increments.

Revision was defined as a case in which the femoral or tibial component had to be removed and cases which were planned for this procedure. Cases in which nettoyage and polyethylene (PE) meniscal replacement took place or cases which were planned for this procedure are defined as reoperation.

Conventional X-rays in anteroposterior and lateral view, taken pre-operative, the first day post-operative and one year post-operative were evaluated on osteoarthritis grade per compartment using the Ahlbäck^[11] (scored from 1 to 5, focusing on narrowing/attrition) by the first author. Progression of osteoarthritis of the lateral or patellofemoral compartment was defined as a change in Ahlbäck score between the X-rays taken the first day-post-operative and one year post-operative.

Statistical analysis

Data were analyzed using SPSS 17 (IBM, New York, United States). Statistical significance was defined as a *P* value < 0.05. Scale variables were tested using the independent samples *t* test. Pearson's χ^2 test was used in case of nominal or ordinal variables.

RESULTS

Of the 99 medial UKP implanted, 53 (53.5%) were cemented UKP and 46 (46.5%) were cementless UKP. Patient characteristics are described in Table 1. The groups were well matched, except for a shorter follow-up time in the cementless group 18.3 mo vs 20.5 mo (*P* = 0.02). This difference was caused by the relatively low volume of cementless UKP implanted in the introduction period.

Reoperations and revisions

During a mean follow-up of 19.5 mo (range 12-33 mo, SD 4.3), seven patients were eligible for reoperation (7%) and three revisions tot TKP were performed (3%). An overview of reoperations and revisions is given in Table 2. The main reason for reoperation was bony or soft-tissue impingement in four cases (4.1%). In two cases (2.0%) subluxation of the meniscal bearing and in one case (1.0%) a 90 degrees rotation of the

Table 2 Reoperations, revisions and outcome

Type	Fixation	Operation performed	Indication	Survival (mo)	Gender	Age (yr)	ASA	BMI kg/m ²	OKS	AKSS O/S
Revision	C	TKP PS 5/5/15 mm	Malrotation tibial component	16	Male	50	1	30.0	-	-
Redo	CL	Nettoyage PE 5 to 8	Subluxation PE	19	Male	50	1	30.0	48	100/100
Revision	C	TKP elsewhere	Aseptic loosening tibial component	20	Female	78	1	27.2	-	-
Redo	C	Nettoyage PE 5 to 6	PE luxation 90 degrees	21	Male	60	2	32.8	46	100/100
Redo	CL	Nettoyage PE 5 to 7	Impingement	21	Male	55	3	32.4	37	80/90
Redo	CL	Nettoyage PE 4 to 7	Impingement	21	Male	64	2	31.7	42	90/100
Redo	C	Nettoyage PE 4 to 6	Subluxation PE	22	Male	51	2	28.4	48	95/100
Redo	CL	Planned	Impingement	23	Male	55	2	26.6	-	-
Redo	CL	Planned	Impingement	26	Female	62	2	25.8	-	-
Revision	C	ACS 5/5/12, 5 mm	Progression of OA lateral/PF	27	Male	51	2	36.3	-	-

BMI: Body mass index; OA: Osteoarthritis; C: Cemented; CL: Cementless; PE: Polyethylene meniscus; OKS: Oxford knee score; AKSS O/S: American knee society score objective score/subjective score.

meniscal bearing occurred. Reoperations were treated with a minimal invasive medial arthrotomy, using the old incision. The impinging osteophytes were removed with a small osteotome, the presence of posterior osteophytes was checked with a curved osteotome and excessive fibrotic tissue was removed. In all cases a thicker PE meniscus was necessary to gain the appropriate balance. The clinical outcome of the reoperations, which were performed more than 6 mo ago, were all good to excellent (Table 2). Statistically, patients with a reoperation were significant younger than patients in the primary group (56.7 vs 64.0, $P = 0.01$) and were more likely to be male (85.7% vs 38.8%, $P = 0.015$). There were no significant differences between the primary group and the redo group concerning body mass index (BMI), ASA classification, SF-12 scores and pre-operative or post-operative OA grade.

All three revisions (3.1%) to TKP were cemented Oxford UKP. Reasons for revision were malrotation of the tibial component, aseptic loosening of the tibial component (revision surgery was performed elsewhere) and progression of OA in the lateral- and patellofemoral compartment. The time to revision was 16, 20 and 27 wk post-implantation. There were no significant differences between the primary group and the revision group concerning age, gender, BMI, ASA classification, SF-12 scores and pre-operative or post-operative Ahlback score.

Functional outcome

The revisions and reoperations excluded, 89 of the original UKP were still *in situ* and eligible for clinical assessment. Although no significant differences were found, the scores were slightly better in the cementless

group, with a VAS pain score of 7.4 vs 11.7 ($P = 0.22$), an OKS of 43.3 vs 41.7 ($P = 0.27$) and a Kujala score of 79.6 vs 78.0 ($P = 0.63$) (Figure 1).

Because of health issues three patients accounting for four medial UKP were not able to come to our clinic for clinical evaluation. One patient refused clinical evaluation because of personal reasons. All these patients had good to excellent OKS outcomes (48, 48, 48 and 38). Of the remaining 85 medial UKP, 44 UKP (51.2%) were cemented and 41 (48.8%) were cementless UKP. The AKSS scores were slightly better in the cementless group 94.5 vs 90.2 ($P = 0.055$) for the objective score and 91.2 vs 87.8 ($P = 0.25$) for the subjective score, both not significantly different (Figure 1). The SF-12 scores were not significantly different in the cementless group, with a mean Physical Component Summary (PCS) score of 49.5 vs 47.6 ($P = 0.28$) and Mental Component Summary (MCS) score of 55.3 vs 54.5 ($P = 0.60$).

Complications

There were no cases of thrombosis or deep infection. No vascular or neurological complications occurred. No fractures were observed post-operatively in this cohort. One patient experienced a length difference of the operated leg after a total hip replacement, which resulted in an inappropriate gait pattern and led to pain in the knee in which the medial UKP was implanted (VAS score 76, OKS 9, Kujala 26).

DISCUSSION

With this cross-sectional study we wanted to compare the short-term clinical outcomes of the cemented and the cementless Oxford phase III medial UKP performed

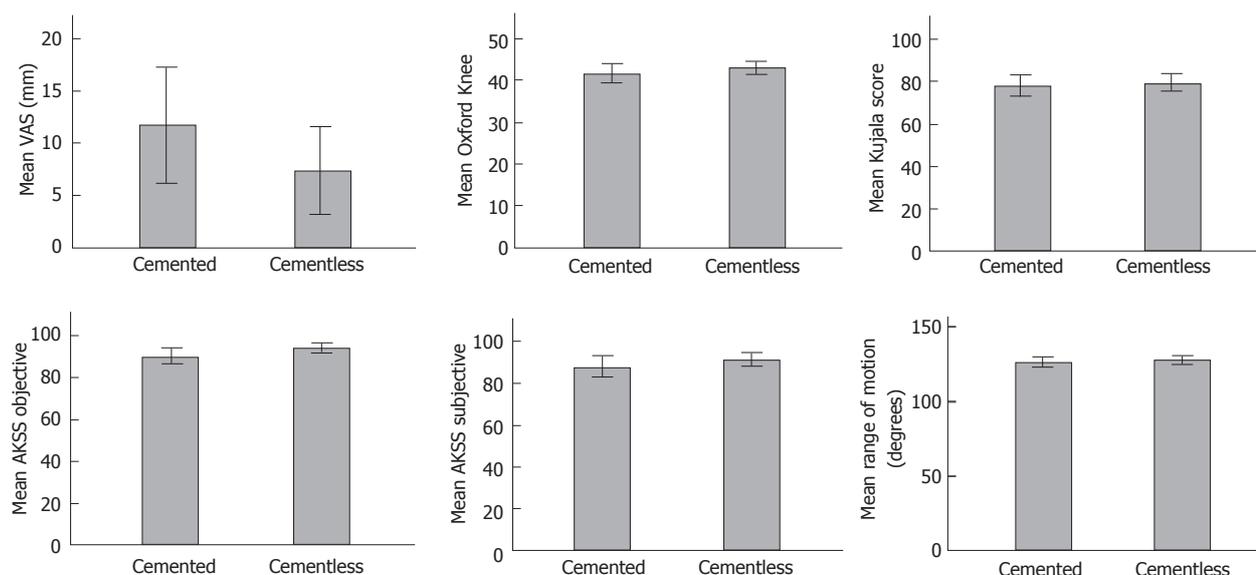


Figure 1 Questionnaire and clinical outcome (mean score with 95%CI error bars).

in an independent center by one single surgeon. We achieved a good to excellent short-term clinical outcome of both the cemented and the cementless Oxford UKP. Although not significant different, the cementless UKP showed better clinical results compared to the cemented UKP. These results support the good clinical results of the Oxford study group^[12,13].

In three cases (sub)luxation of the PE bearing occurred. PE bearing exchange with a good clinical outcome was not considered as a revision, but was listed as a reoperation (Table 2). In four cases the patient experienced impingement of the PE bearing, because of bony- or soft tissue re-growth at the bone ridge cranial to the anterior side of the femur condyle.

Patients requiring a reoperation were significantly younger and more frequently male. In earlier Oxford UKP survival studies gender has shown not to affect UKP survival. Whether age under 60 years old influences the survival rates is still a discussion. The Oxford group has shown in their studies no significant difference between survival in patients under and over 60 years old^[13]. Worldwide registers and other independent studies however show higher revision rates in patients under 60 years old^[14-16]. Patients aged under 60 in the reoperation group were relatively active patients, which we think might be part of the explanation for (sub)luxation. Impingement might be caused by too little bone resection cranial to the anterior side of the femur component or because of re-growth. We currently use the microplasty instrumentation and aim for a resection of approximately 10 mm caudal to the femur component, which seems to reduce the amount of patients with signs of anterior impingement.

Based on our results and experience, we believe that if there is an obvious reason for pain in a medial UKP, a reoperation can be successful and it prevents (early) revision surgery. This does require accurate patient

selection, based on physical examination and radiologic reviewing by an experienced surgeon.

There were no revisions in the cementless group. Of the cemented UKP, three had to be revised to a TKP, two of these revisions were performed in our clinic. Reasons for revision were malposition, aseptic loosening of the tibia component and progression of OA in the lateral and patellofemoral compartments. The time to revision varied between 16-27 mo. Two of the revisions were performed within the first two years after implantation. Generally, it is not recommended to revise a medial UKP to a TKP in the first two years after implantation, because of tibial stress and the bone remodeling that occurs. In this phase, medial pain is common and a bone scintigraphy can show false-positive results. Unless there is an obvious reason for failure of the UKP, revision to a TKP in this phase can be unsatisfying^[13].

The revision rates of the cemented UKP lie in between the excellent results of the Oxford study group^[13] and the Joint registry reports^[17].

Surgical errors play a considerable role in UKP failure, as over-correction of an existing valgus deformity, overstuffing and cementing technique are frequently reported reasons for revision^[17]. With the cementless UKA, cementing errors such as uneven distribution of the cement, cement residue posterior and loose particles, are eliminated. It is also known that cemented medial UKP show physiological radiolucent lines at follow-up, a phenomenon that is less seen in the cementless medial UKP^[3]. Physiological radiolucent lines after medial UKP can easily be mistaken for radiolucency due to aseptic loosening. These factors may contribute to lower revision rate in cementless medial UKP compared to cemented medial UKP^[1].

The cementless UKP needs an adequate initial fixation. Although not observed in this cohort, peri-prosthetic tibia plateau fractures are more frequently

observed in cementless UKP. This might be due to a deep posterior tibial cortical cut or due to hard hammering, both should be avoided.

The strength of this study is the specialized character of our clinic and the choice to only include patients operated by one single surgeon. The occurrence of surgical errors is related to the frequency of the operation performed and the experience of the surgeon and his staff¹⁷. Our clinic is specialized in sports-, arthroscopic- and prosthetic surgery. We perform approximately 200 UKP per year of which more than half are performed by the senior author (Marcel JM Driessen). By comparing the clinical outcome of the cemented and cementless UKP performed by a single surgeon, we eliminated a surgeon bias for indication as well as a bias in surgical technique. Limitations of this study are the cross-sectional design and the relatively short follow-up time.

The cementless Oxford phase III medial UKP shows promising short-term clinical outcome when used in a specialized orthopedic center. Because of the promising results of the cementless Oxford phase III medial UKP, it is now the most used medial UKP in our clinic for eligible patients.

ACKNOWLEDGMENTS

We would like to thank Arne Heneweer MSc. for biostatistical review.

COMMENTS

Background

The unicondylar knee prosthesis (UKP) is an established treatment for end-stage osteoarthritis (OA) of the knee and accounts for around 8%-10% of all primary knee replacements. One of the successful implants used, is the cemented Oxford medial UKP phase III. This is a fully congruent mobile bearing prosthesis, which is implanted via a minimal invasive procedure with minimal bone-loss. The success of the medial UKP is still largely related to the indication for surgery and the experience of the surgeon and the surgical team. The higher revision rates in unicondylar arthroplasty are a concern. The difference in revision rate between a UKP and a total knee prosthesis (TKP) is likely to be multi-factorial. A major issue seems to be the ease of choosing for a revision of a UKP compared to a TKP.

Research frontiers

The developing hospital has published encouraging results of the cementless Oxford phase III medial UKP, as well has cementless UKP by other manufacturers.

Innovations and breakthroughs

With the introduction of the cementless Oxford UKP (2003) one of the technical errors related to failure, the cementing technique can be eliminated. Also, the cementless Oxford medial UKP shows reduced radiolucent lines at one year follow-up, whereas the cemented Oxford medial UKP shows occurrence of radiolucent lines during follow-up. The occurrence of radiolucent lines is thought to be a misleading factor for revision in patients with unexplained pain after cemented UKP. In accordance with earlier published results, it is our experience that the cementless Oxford UKP performs as well as, or even better than the cemented Oxford UKP.

Applications

With this retrospective study the authors want to compare the short-term clinical outcome of the cemented and the cementless Oxford phase III medial UKP

performed in an independent center by one single surgeon.

Peer-review

This is a good article.

REFERENCES

- 1 **Robertsson O**, Knutson K, Lewold S, Lidgren L. The routine of surgical management reduces failure after unicompartmental knee arthroplasty. *J Bone Joint Surg Br* 2001; **83**: 45-49 [PMID: 11245537]
- 2 **Koskinen E**, Paavolainen P, Eskelinen A, Pulkkinen P, Remes V. Unicondylar knee replacement for primary osteoarthritis: a prospective follow-up study of 1,819 patients from the Finnish Arthroplasty Register. *Acta Orthop* 2007; **78**: 128-135 [PMID: 17453404]
- 3 **Pandit H**, Jenkins C, Beard DJ, Gallagher J, Price AJ, Dodd CA, Goodfellow JW, Murray DW. Cementless Oxford unicompartmental knee replacement shows reduced radiolucency at one year. *J Bone Joint Surg Br* 2009; **91**: 185-189 [PMID: 19190051 DOI: 10.1302/0301-620X.91B2.21413]
- 4 **Saxler G**, Temmen D, Bontemps G. Medium-term results of the AMC-unicompartmental knee arthroplasty. *Knee* 2004; **11**: 349-355 [PMID: 15351408]
- 5 **Forsythe ME**, Englund RE, Leighton RK. Unicondylar knee arthroplasty: a cementless perspective. *Can J Surg* 2000; **43**: 417-424 [PMID: 11129829]
- 6 **Magnussen PA**, Bartlett RJ. Cementless PCA unicompartmental joint arthroplasty for osteoarthritis of the knee. A prospective study of 51 cases. *J Arthroplasty* 1990; **5**: 151-158 [PMID: 2358814]
- 7 **Haverkamp D**, Breugem SJ, Sierevelt IN, Blankevoort L, van Dijk CN. Translation and validation of the Dutch version of the Oxford 12-item knee questionnaire for knee arthroplasty. *Acta Orthop* 2005; **76**: 347-352 [PMID: 16156462]
- 8 **Kujala UM**, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy* 1993; **9**: 159-163 [PMID: 8461073]
- 9 **Gandek B**, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998; **51**: 1171-1178 [PMID: 9817135]
- 10 **Van Der Straeten C**, Witvrouw E, Willems T, Bellemans J, Victor J. Translation and validation of the Dutch new Knee Society Scoring System ©. *Clin Orthop Relat Res* 2013; **471**: 3565-3571 [PMID: 23836243 DOI: 10.1007/s11999-013-3149-6]
- 11 **Ahlbäck S**. Osteoarthritis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968; **Suppl 277**: 7-72 [PMID: 5706059]
- 12 **Pandit H**, Liddle AD, Kendrick BJ, Jenkins C, Price AJ, Gill HS, Dodd CA, Murray DW. Improved fixation in cementless unicompartmental knee replacement: five-year results of a randomized controlled trial. *J Bone Joint Surg Am* 2013; **95**: 1365-1372 [PMID: 23925740 DOI: 10.2106/JBJS.L.01005]
- 13 **Liddle AD**, Pandit H, O'Brien S, Doran E, Penny ID, Hooper GJ, Burn PJ, Dodd CA, Beverland DE, Maxwell AR, Murray DW. Cementless fixation in Oxford unicompartmental knee replacement: a multicentre study of 1000 knees. *Bone Joint J* 2013; **95-B**: 181-187 [PMID: 23365026 DOI: 10.1302/0301-620X.95B2.30411]
- 14 **Kuipers BM**, Kollen BJ, Bots PC, Burger BJ, van Raay JJ, Tulp NJ, Verheyen CC. Factors associated with reduced early survival in the Oxford phase III medial unicompartment knee replacement. *Knee* 2010; **17**: 48-52 [PMID: 19716706 DOI: 10.1016/j.knee.2009.07.005]
- 15 **Matharu G**, Robb C, Baloch K, Pynsent P. The Oxford medial unicompartmental knee replacement: survival and the affect of age and gender. *Knee* 2012; **19**: 913-917 [PMID: 22480781 DOI: 10.1016/j.knee.2012.03.004]
- 16 **Kort NP**, van Raay JJ, van Horn JJ. The Oxford phase III

unicompartmental knee replacement in patients less than 60 years of age. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 356-360 [PMID: 17028868]

17 **Label G**, Sekyra K, Pawelka W, Janda W, Stöckl B. Outcome and

reproducibility of data concerning the Oxford unicompartmental knee arthroplasty: a structured literature review including arthroplasty registry data. *Acta Orthop* 2011; **82**: 131-135 [PMID: 21434760 DOI: 10.3109/17453674.2011.566134]

P- Reviewer: Gill TK **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Wu HL



Retrospective Cohort Study

Ankle fracture configuration following treatment with and without arthroscopic-assisted reduction and fixation

Chayanin Anghong

Chayanin Anghong, Department of Orthopaedics, Faculty of Medicine, Thammasat University, Klong Luang 12120, Pathum Thani, Thailand

Author contributions: Anghong C designed and performed the research, analyzed the data and wrote the paper.

Institutional review board statement: This study (study code: MTU-EC-OT-0-099/54) was approved by the institutional review board of the Faculty of Medicine, Thammasat University, Pathum Thani, Thailand.

Informed consent statement: All involved participants gave their informed consent prior to study inclusion.

Conflict-of-interest statement: The author received the funding supports for academic meetings and visit from Smith and Nephew LTD (Thailand) and Device Innovation (Arthrex distributor in Thailand).

Data sharing statement: The original dataset is available on request from the corresponding author at chatthara@yahoo.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Chayanin Anghong, MD, PhD, Department of Orthopaedics, Faculty of Medicine, Thammasat University, Klong Luang 12120, Pathum Thani, Thailand. chatthara@yahoo.com
Telephone: +66-2-9269775
Fax: +66-2-9269793

Received: May 9, 2015
Peer-review started: May 11, 2015
First decision: July 27, 2015
Revised: December 10, 2015

Accepted: January 5, 2016
Article in press: January 7, 2016
Published online: April 18, 2016

Abstract

AIM: To report ankle fracture configurations and bone quality following arthroscopic-assisted reduction and internal-fixation (ARIF) or open reduction and internal-fixation (ORIF).

METHODS: The patients of ARIF ($n = 16$) or ORIF ($n = 29$) to treat unstable ankle fracture between 2006 and 2014 were reviewed retrospectively. Baseline data, including age, sex, type of injury, immediate postoperative fracture configuration (assessed on X-rays and graded by widest gap and largest step-off of any intra-articular site), bone quality [assessed with bone mineral density (BMD) testing] and arthritic changes on X-rays following surgical treatments were recorded for each group.

RESULTS: Immediate-postoperative fracture configurations did not differ significantly between the ARIF and ORIF groups. There were anatomic alignments as 8 (50%) and 8 (27.6%) patients in ARIF and ORIF groups ($P = 0.539$) respectively. There were acceptable alignments as 12 (75%) and 17 (58.6%) patients in ARIF and ORIF groups ($P = 0.341$) respectively. The arthritic changes in follow-up period as at least 16 wk following the surgeries were shown as 6 (75%) and 10 (83.3%) patients in ARIF and ORIF groups ($P = 0.300$) respectively. Significantly more BMD tests were performed in patients aged > 60 years ($P < 0.001$), ARIF patients ($P = 0.021$), and female patients ($P = 0.029$). There was no significant difference in BMD test t scores between the two groups.

CONCLUSION: Ankle fracture configurations following

surgeries are similar between ARIF and ORIF groups, suggesting that ARIF is not superior to ORIF in treatment of unstable ankle fractures.

Key words: Arthroscopy; Ankle; Fractures; Fracture fixation; Bone densitometry reports

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: There was no significant difference between arthroscopic-assisted reduction and internal-fixation (ARIF) and open reduction and internal-fixation (ORIF) in immediate-postoperative ankle fracture configuration in the present study. Although the use of arthroscopy in orthopaedic trauma is increasing, the effectiveness of ARIF compared with that of ORIF in the management of ankle fractures has yet to be verified. The low rate of bone mineral density testing reflects a lack of awareness of the need for routine post-injury testing for osteoporosis in patients with ankle fractures.

Angthong C. Ankle fracture configuration following treatment with and without arthroscopic-assisted reduction and fixation. *World J Orthop* 2016; 7(4): 258-264 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/258.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.258>

INTRODUCTION

Ankle arthroscopy, introduced into the field of ankle surgery for several years is a minimally invasive intra-articular treatment with several advantages^[1,2]. Miyamoto *et al*^[3] reported the benefit of arthroscopic examination in the diagnosis of syndesmotic disruption, which occurs mostly with ankle fracture. Imade *et al*^[4] also demonstrated the advantages of arthroscopic procedures for ankle injury combined with Maisonneuve fracture, such as arthroscopic-assisted visualization during syndesmotic screw fixation, and drilling an osteochondral lesion of the talus. Takao *et al*^[5] proposed the role of arthroscopic-assisted reduction and internal fixation for accurate diagnose and treat intra-articular disorders combined with distal fibular fractures. However, there are no reports of fracture configuration and bone quality in patients with unstable ankle fractures treated with arthroscopic-assisted reduction and internal fixation (ARIF) vs open reduction and internal fixation (ORIF).

To address this, the immediate-postoperative configurations of intra-articular ankle fractures, as well as bone quality *via* postoperative bone mineral density (BMD) testing, were investigated in a series of unstable ankle fractures treated with ARIF or ORIF. Relationships between relevant patient and technical variables and postoperative BMD were also determined. The study tested the hypothesis that there was no

Table 1 Patients' baseline data

	Arthroscopic-assisted reduction and internal fixation	Open reduction and internal fixation	P value
Number	16	29	
Age (yr) ¹	47.8 ± 16.3	45.0 ± 16.8	0.590
Male/female	5/11	19/10	0.035 ²
Lauge-Hansen	14/2	19/10	0.164
Supination/pronation			
Bone mineral density test	7 (43.8%)	3 (10.3%)	0.021 ²

¹Mean ± SD; ²Significant difference.

difference between ARIF and ORIF; the alternative, that ARIF is superior to ORIF in the treatment of unstable ankle fracture, would be demonstrated by associations between ARIF and superior anatomic fracture configuration. A second aim of the study was to determine the prevalence of post-injury BMD testing in order to evaluate clinicians' level of awareness regarding the need for investigation of osteoporosis in patients with ankle fractures.

MATERIALS AND METHODS

The medical records of patients who underwent fixation of unstable ankle fractures between April 2006 and October 2014 were reviewed retrospectively. After the exclusion of patients with incomplete or unavailable medical records or inadequate radiographic data, 45 ankle fractures in 45 patients [mean age, 46.5 years (range, 18-80 years)] were included in the study. ARIF (*n* = 16) or ORIF (*n* = 29) had been performed at the discretion of the attending surgeon. Thirty-three patients (73.3%) had a supination-type^[6] ankle fracture and 12 (26.7%) had pronation-type^[6] ankle fracture. Baseline data, including demographic information, and the rate of BMD testing, are presented in Table 1. This study was approved by the institutional review board of the medical center where this study (study code: MTU-EC-OT-0-099/54) was performed.

Operative technique

Before each procedure, the operated limb was exsanguinated and a thigh tourniquet was inflated to 250-300 mmHg and deflated after wound closure. All patients in the ARIF group were operated on by the same foot-ankle arthroscopy fellowship-trained surgeon (CA). Fracture configuration was checked after fixation by fluoroscopic and arthroscopic examination and corrected, whenever possible, if the alignment was not acceptable. As recommended by Miyamoto *et al*^[3], direct visualization *via* arthroscopy was achieved with the use of fluid irrigation *via* gravity flow (*i.e.*, without a pump), through the anterolateral and anteromedial portals. Arthroscopic assessment was performed after fixation in order to evaluate the stability of the distal



Figure 1 The immediate-postoperative fracture configuration via the radiograph in the arthroscopic-assisted reduction and internal fixation group.

tibiofibular syndesmosis, with fixation considered inadequate if an opening of 2 mm could be identified, and to identify and debride any fibrous tissue interposed in the distal tibiofibular joint. Any other intra-articular disorders, such as osteochondral injury and synovitis, which often accompany unstable ankle fracture, were accessed and treated at that time.

In the ORIF group, patients were operated on by the author, other orthopaedic trauma surgeons, or fellowship-trained foot-ankle surgeons. Anteromedial approach was used for medial malleolar reduction and fixation. The reduction was mainly confirmed by the apposition of fracture ridge at the outer rim of ankle joint and not the direct vision in the joint space. It was also confirmed by the fluoroscopic examination. Lateral approach was used for lateral malleolar or distal fibular reduction and fixation. The reduction was mainly confirmed by the apposition of fracture ridge at the outer rim of ankle joint and not the direct vision in the joint space. It was also confirmed by the fluoroscopic examination. The final configuration of fractures and alignments was checked by fluoroscopic examination after all fixation(s) and, if the alignment was not acceptable, corrected if possible. Surgical drains, including a drain set to bulb suction or a Penrose drain, were placed prior to closing the wound at the discretion of the attending surgeon. A posterior short leg splint was applied after wound closure in all cases.

Radiographic outcome

For all patients, independent evaluations of plain radiographs (anteroposterior, mortise, and lateral views) were conducted by trained orthopedic interns to determine immediate-postoperative fracture configuration and arthritic changes following the surgeries. Assessment of step-off and the widest gap at any intra-articular site of fracture involvement was graded according to the following scales: (1) Detailed evaluation of step-off/gap: Fracture configuration was considered anatomic for a step-off/gap of ≤ 1.0 mm, good for 1.1-2.0 mm, fair for 2.1-3.0 mm; and poor for > 3.0 mm); (2) General evaluation of step-off/gap: Fracture configuration was also assigned a general grade of either

acceptable (step-off/gap ≤ 2.0 mm) or unacceptable (step-off/gap > 2.0 mm).

Statistical analysis

Data were analyzed using SPSS for Windows, Version 13.0 (SPSS Inc., Chicago, IL, United States). Categorical variables were compared using the Fisher's exact test or χ^2 test, and continuous variables were compared using Student's *t* test for normally distributed data or the Mann-Whitney *U* test for non-normally distributed data. A *P* value of < 0.05 was considered statistically significant.

RESULTS

Neither group demonstrated compartment syndrome or significant complications postoperatively. Table 1 presents a comparison of demographic and clinical variables between the ARIF and ORIF groups. The ARIF and ORIF groups did not differ significantly in age or fracture type (Lauge-Hansen supination/pronation^[6]). However, there were significantly more female patients in the ARIF group than in the ORIF group ($P = 0.035$), and significantly more ARIF patients than ORIF patients underwent post-injury BMD testing ($P = 0.021$).

Table 2 presents radiographic outcomes for both groups. There was no significant difference in immediate-postoperative fracture configuration, as assessed by both detailed and general grading systems, between the ARIF (Figure 1) and ORIF (Figure 2) groups. Regarding the arthritic changes of ankle following the fracture, there were 20 patients who had the follow-up period as at least 16 wk following the surgeries (mean follow-up time: 9.8 mo; range 4-22 mo). There were 16 patients (80%) who had mild to significant level of arthritic changes (Table 3). In addition, there were no significant difference of the rates of arthritic changes between ARIF and ORIF groups ($P = 0.3$) (Table 3). Regarding the postoperative complications, there were two patients who had the available records reporting postoperative complications in overall study (ORIF group: 1 patient with major complications needing additional surgeries; ARIF group: 1 patient with a general complication

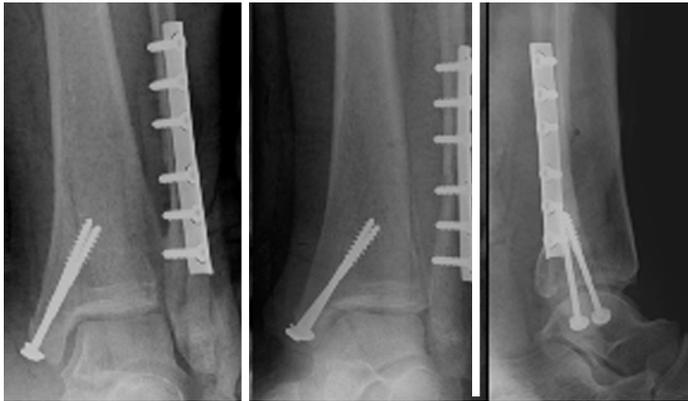


Figure 2 The immediate-postoperative fracture configuration via the radiograph in the open reduction and internal fixation group.

	Arthroscopic-assisted reduction and internal fixation	Open reduction and internal fixation	P value
Meticulous grading			
Anatomic (step/gap ≤ 1.0 mm)	8 (50%)	8 (27.6%)	0.539
Good (step/gap = 1.1-2.0 mm)	4 (25%)	9 (31.0%)	
Fair (step/gap = 2.1-3.0 mm)	2 (12.5%)	5 (17.2%)	
Poor (step/gap > 3.0 mm)	2 (12.5%)	7 (24.1%)	
General grading			
Acceptable (step/gap ≤ 2.0 mm)	12 (75.0%)	17 (58.6%)	0.341
Unacceptable (step/gap > 2.0 mm)	4 (25.0%)	12 (41.4%)	

Treatment groups	Arthritic changes ¹			Significance	P value
	None	Mild	Moderate		
Arthroscopic-assisted reduction and internal fixation	2 (25%)	3 (37.5%)	0	3 (37.5%)	0.3
Open reduction and internal fixation	2 (16.7%)	6 (50%)	3 (25%)	1 (8.3%)	
Total	4 (20%)	9 (45%)	3 (15%)	4 (20%)	

¹Arthritic changes was described as mild (presence of osteophyte), moderate (narrowing of joint space), and significance (presence of osteophyte associated with narrowing of joint space).

with no need of additional surgeries). In ORIF group, a mentioned patient had major complications as malaligned fracture and loss of reduction following the initial surgery. In the retrospective review of his initially postoperative radiograph, there was the non-anatomic reduction of medial malleolar fracture with a fracture gap around 1.4 mm (Figure 3) but it was missed during the procedure. He also had the surgical wound inflammation and possible infection that needed the surgical debridement and hardware removal. He was treated with an ankle arthrodesis as a definitive procedure. He could return to recovery uneventfully following the final treatment. In ARIF group, a mentioned patient had a general complication as the surgical wound inflammation and possible infection that needed only intravenous antibiotic medication and local wound care. Her wound had been healed uneventfully following the mentioned treatment. Both major and general complications rates were no significant differences between the two groups ($P > 0.05$).

Table 4 compares demographic, clinical, and perioperative data for patients who did and did not undergo BMD testing. Of the 45 study patients, only 10 (22.2%) underwent post-injury BMD testing; 8 of 10 BMD-tested patients had a t score indicative of osteopenia^[7,8]. There were significantly higher rates of BMD testing in patients aged > 60 years ($P < 0.001$), patients who underwent ARIF ($P = 0.021$), and female patients ($P = 0.029$).

However, bone quality, as assessed by BMD-test t scores, did not differ significantly between the ARIF and ORIF groups. In addition, no significant difference was found in the prevalence of BMD testing between low- and high-energy-fractures ($P = 0.341$) or among the differences of postoperatively fracture configurations ($P = 0.06$).

Subgroup analysis of the arthroscopic findings of patients in the ARIF group is presented in Table 5. Osteochondral lesion of the tibial plafond (modified Outerbridge grade II^[9]) was found in one patient. The most common locations of talar lesions were the anterolateral (37.6%) and anteromedial (18.8%) areas. Sixty percent of microfractures as described by previous authors^[1] were performed for grade III-IV osteochondral lesions.

DISCUSSION

Over the past decade, the number of orthopedic surgical procedures performed with arthroscopic assistance has increased^[3-5]. Indications for ARIF include transchondral talar dome fracture, talar fracture, low-grade fracture of the distal tibia, syndesmotic injury, malleolar fracture, and chronic pain following definitive management of fracture about the ankle^[3-5,10]. Among

Table 4 Bone mineral density test and related parameters

	Patients with BMD tests (n = 10)	Patients without BMD tests (n = 35)	P value
Age (yr) ¹	64.2 ± 9.4	40.8 ± 14.3	< 0.001 ²
Male/female	2/8	22/13	0.029 ²
Lauge-Hansen	9/1	24/11	0.246
Supination/pronation			
ORIF/ARIF	3/7	26/9	0.021 ²

¹Mean ± SD; ²Significant difference. ARIF: Arthroscopic-assisted reduction and internal fixation; BMD: Bone mineral density; ORIF: Open reduction and internal fixation.

Table 5 Arthroscopic findings in arthroscopic-assisted reduction and internal fixation patients

Findings	Number of patients (%)
Osteochondral lesions	
Talus	10 (62.5%)
Tibial plafond	1 (6.3%)
Modified outerbridge classification (talar lesion)	
Grade I	1 (6.3%)
Grade II	4 (25%)
Grade III	3 (18.8%)
Grade IV	2 (12.5%)
Synovitis	15 (93.7%)
Lateral	1 (6.3%)
Medial and lateral	11 (68.8%)
Unspecified	3 (18.8%)
Ligamentous injury	
None	6 (37.5%)
AITFL	6 (37.5%)
AITFL-PITFL	2 (12.5%)
AITFL-Deep deltoid	2 (12.5%)

ARIF: Arthroscopic-assisted reduction and internal fixation; AITFL: Anteroinferior tibiofibular ligament; PITFL: Posteroinferior tibiofibular ligament.

the potential benefits are less extensive exposure, preservation of blood supply, and improved visualization of the pathology. However, data regarding fracture configuration and bone quality in patients with unstable ankle fractures treated with and without ARIF have not been reported.

The present study demonstrates no significant difference in immediate-postoperative configuration or arthritic changes in a short-term follow-up period between groups. Other authors^[5], however, have previously shown superior results in the ARIF group. With regard to between-group differences in postoperative fracture configuration, the discrepancy between our results and those of other authors^[5] may have been the result of the small number of patients in the ARIF group in the present study. Future prospective studies that include larger numbers of patients with longer term of follow-up and in which clinical scores are recorded in conjunction with the evaluation of postoperative fracture configuration and arthritic changes are necessary to determine whether there



Figure 3 The initially postoperative radiograph revealed the non-anatomic reduction of medial malleolar fracture with a fracture gap around 1.4 mm which was missed during the primary procedure in the open reduction and internal fixation group.

is a significant association between ARIF and better postoperative outcomes. However, as an alternative to conventional osteosynthesis, ARIF can facilitate correct assessment of surgical reduction of complex fractures and allow visualization of non-anatomical reductions that would not otherwise be detected under fluoroscopy^[11]. This may help to minimize surgical soft-tissue damage and wound extension during surgical reduction^[11,12]. Moreover, intra-articular pathology and associated cartilaginous lesions, such as those detected in the present study, can be evaluated and treated as appropriate^[11,13].

Regarding the comparison of advantages and disadvantages between ARIF and conventional osteosynthesis or ORIF, the advantages of ARIF were demonstrated as it could directly assess a reduction of an intra-articular fracture and this could provide more anatomic reduction than ORIF. In addition, this procedure was able to perform the debridement to remove the residual hematoma and synovitis debris that might cause pain and limitation of an ankle motion after fixation. It could perform the arthroscopic repair of concomitant injury such as osteochondral lesions^[11,13]. Finally, it could also help the surgeon to evaluate syndesmotic widening from the syndesmotic injury during the arthroscopic examination^[3] and following syndesmotic fixation if this injury was associated with an ankle fracture. The disadvantages of ARIF could be informed as it might considerably add the operative time by the surgeon with an inadequacy of arthroscopic skills. The longer time of operation might potentially lead to the swelling of surgical wound and compartment syndrome, particularly in some types of ankle fractures such as a Maisonneuve fracture^[4]. On the other hand, the advantages of ORIF were explained, as this approach was familiar with any surgeons who had basic skills of the open reduction and fixation of fracture. There was no need of arthroscopic skills to perform this conventional approach. Therefore, this approach is more reproducibility than ARIF. In addition, it has low risk of the compartment syndrome following the operation.

However, the disadvantages of ORIF could be as the inability to directly confirm the anatomic reduction of fractures in the joint space. The reduction was routinely checked by the apposition of fracture ridge at the outer rim of ankle joint and by the fluoroscopic examination. These methods could miss some subtle malreduction of fracture in the joint^[11] as shown in one patient in ORIF group in the present study. This approach could not perform directly debridement of the residual hematoma included another debris in the joint. It could not perform simultaneously repair of associated lesions, such as osteochondral lesions, or directly assess the syndesmotic widening during the procedure. Surgeons may have to consider these advantages and disadvantages of each approach when they have to make any decision for their patients.

In the present study, only 22.2% of patients received a post-injury BMD test. This suggests a lack of awareness of the need for routine post-injury testing for osteoporosis in ankle-fracture patients; particularly those over the age of 45 (mean age of patients in the present study was 46.5 years). This lack of awareness is consistent with the same parameter in overall low-or high energy fractures in a previous study^[7]. No significant difference was found in the prevalence of BMD testing between patients with low and high-energy fractures ($P = 0.341$) or among the grades of postoperative fracture configuration ($P = 0.06$). However, age > 60 years and female sex were identified in the present study to be factors significantly associated with post-fracture BMD testing. In ARIF patients, in-patient care by a single foot-ankle surgeon was a significant predictor of post-fracture BMD. Castel *et al*^[14] proposed that many physicians do not recognize osteoporosis as a metabolic condition and thus fail to correlate it with other medical conditions. Suarez-Almazor *et al*^[15] revealed that physician attitudes were vital factors in decisions about screening and treatment of osteoporosis. Female patients were more likely than male patients to receive BMD testing after a low-energy fracture^[7]. Castel *et al*^[14] proposed that this bias might be due to the misapprehension that osteoporosis is a problem affecting only females. Improved communication between orthopedic surgeons, specialists, and involved physicians with respect to evidence-based medicine may help to reduce the gap between fracture occurrence and osteoporosis management in both sexes.

In the present study, eight patients in a subgroup of 10 BMD-tested patients had t scores indicative of osteopenia^[4,5]. It has been suggested that there is an association between vitamin D deficiency and osteoporosis^[16]. The high rate of osteopenia in the present study is consistent with that of a previous study, which demonstrated vitamin D deficiency to be common among patients with foot or ankle fracture^[17]. These studies highlight the importance of diagnosing osteoporosis in patients with ankle fractures, particularly in patients who have low energy fractures, in order to

prevent subsequent fractures^[18,19]. A limitation of the present study was that the small number of patients in the ARIF group might have made a between-group difference difficult to detect.

In conclusion, there was no significant difference between ARIF and ORIF in immediate-postoperative ankle fracture configuration or arthritic changes in a short-term follow-up period. Further study with larger number of patients and longer term of follow-up was needed to validate this conclusion. Although the use of arthroscopy in trauma is increasing, the effectiveness of ARIF compared with that of ORIF in the management of ankle fractures has yet to be verified. The low rate of BMD testing reflects a lack of awareness of the need for routine post-injury testing for osteoporosis in patients with ankle fractures.

ACKNOWLEDGMENTS

The author would like to propose special thanks to Dr. Waroot Pholsawatthai and Dr. Artit Ngiemsuwan who supported about data collection in this study.

COMMENTS

Background

Ankle arthroscopy, introduced into the field of ankle surgery for several years is a minimally invasive intra-articular treatment with several advantages. However, there are no reports of fracture configuration, bone quality, arthritic changes in patients with unstable ankle fractures treated with arthroscopic-assisted reduction and internal fixation (ARIF) vs open reduction and internal fixation (ORIF).

Research frontiers

The present study is to report ankle fracture configurations, bone quality, and arthritic changes following ARIF or ORIF.

Innovations and breakthroughs

In the past, some concerns arose about safety and efficacy of ARIF. In addition, some surgeons may concern it as difficult to perform for the routinely practice basis. The present study shows that ARIF is comparable to ORIF in terms of postoperative results as immediate-postoperative ankle fracture configuration or arthritic changes or complication rates in a short-term follow-up period. However, ARIF could directly assess a reduction of an intra-articular fracture or syndesmosis and this may provide more anatomic reduction than ORIF in larger study. In addition, arthroscopic treatments for associated intra-articular lesions can be performed in patients with ARIF. This kind of procedure is the advantage in the ARIF group.

Applications

Patients with unstable ankle fractures will benefit from ARIF, if treated with cautiously systematic steps as described in the section of operative technique, avoiding untreated intra-articular lesions which commonly associated with ankle fracture and possibly correlated with long term posttraumatic arthritis.

Terminology

ARIF is referred to the operation that uses an arthroscopic examination to evaluate the stability of the distal tibiofibular syndesmosis, fracture alignment following open reduction and internal fixation, and other intra-articular disorders, such as osteochondral injury and synovitis, which often accompany unstable ankle fracture. The improper alignment of fracture and associated intra-articular lesions can be accessed and treated at that time. ORIF is referred to the conventional operation that uses an open surgery to perform the fracture

reduction and internal fixation. This kind of procedure does not include the arthroscopic examination during the procedure. Bone mineral density (BMD) testing is to measure how much calcium and other types of minerals are in a location of bone in each patient. This test helps the health care provider detect osteopenia or osteoporosis and predict the risk of fractures in each patient. The present study used a dual-energy X-ray absorptiometry scan for the BMD-test which would demonstrate the result in a value of "t score".

Peer-review

It is a well written article and very interesting.

REFERENCES

- 1 **Angthong C**, Yoshimura I, Kanazawa K, Takeyama A, Hagio T, Ida T, Naito M. Critical three-dimensional factors affecting outcome in osteochondral lesion of the talus. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1418-1426 [PMID: 23328985 DOI: 10.1007/s00167-013-2364-8]
- 2 **Zengerink M**, Struijs PA, Tol JL, van Dijk CN. Treatment of osteochondral lesions of the talus: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 238-246 [PMID: 19859695 DOI: 10.1007/s00167-009-0942-6]
- 3 **Miyamoto W**, Takao M. Management of chronic disruption of the distal tibiofibular syndesmosis. *World J Orthop* 2011; **2**: 1-6 [PMID: 22474625 DOI: 10.5312/wjo.v2.i1.1]
- 4 **Imade S**, Takao M, Miyamoto W, Nishi H, Uchio Y. Leg anterior compartment syndrome following ankle arthroscopy after Maisonneuve fracture. *Arthroscopy* 2009; **25**: 215-218 [PMID: 19171284 DOI: 10.1016/j.arthro.2007.08.027]
- 5 **Takao M**, Uchio Y, Naito K, Fukazawa I, Kakimaru T, Ochi M. Diagnosis and treatment of combined intra-articular disorders in acute distal fibular fractures. *J Trauma* 2004; **57**: 1303-1307 [PMID: 15625464 DOI: 10.1097/01.TA.0000114062.42369.88]
- 6 **Lauge-hansen N**. Fractures of the ankle. II. Combined experimental-surgical and experimental-roentgenologic investigations. *Arch Surg* 1950; **60**: 957-985 [PMID: 15411319 DOI: 10.1001/archsurg.1950.01250010980011]
- 7 **Angthong C**, Rodjanawijitkul S, Samart S, Angthong W. Prevalence of bone mineral density testing and osteoporosis management following low- and high-energy fractures. *Acta Orthop Traumatol Turc* 2013; **47**: 318-322 [PMID: 24164940 DOI: 10.3944/AOTT.2013.3065]
- 8 **Levasseur R**, Sabatier JP, Guilcher C, Guaydier-Souquières G, Costentin-Pignol V, Jean-Jacques PY, Hulet C, Vielpeau C, Marcelli C. Medical management of patients over 50 years admitted to orthopedic surgery for low-energy fracture. *Joint Bone Spine* 2007;

- 9 **Uhl M**, Allmann KH, Tauer U, Laubenberger J, Adler CP, Ihling C, Langer M. Comparison of MR sequences in quantifying in vitro cartilage degeneration in osteoarthritis of the knee. *Br J Radiol* 1998; **71**: 291-296 [PMID: 9616238 DOI: 10.1259/bjr.71.843.9616238]
- 10 **Bonasia DE**, Rossi R, Saltzman CL, Amendola A. The role of arthroscopy in the management of fractures about the ankle. *J Am Acad Orthop Surg* 2011; **19**: 226-235 [PMID: 21464216]
- 11 **Schoepp C**, Rixen D. Arthroscopy-guided fracture management. Ankle joint and calcaneus. *Unfallchirurg* 2013; **116**: 318-325 [PMID: 23515645 DOI: 10.1007/s00113-012-2347-0]
- 12 **Kong C**, Kolla L, Wing K, Younger AS. Arthroscopy-assisted closed reduction and percutaneous nail fixation of unstable ankle fractures: description of a minimally invasive procedure. *Arthrosc Tech* 2014; **3**: e181-e184 [PMID: 24749042 DOI: 10.1016/j.eats.2013.09.018]
- 13 **Turhan E**, Doral MN, Demirel M, Atay AO, Bozkurt M, Bilge O, Huri G, Atesok K, Kaya D. Arthroscopy-assisted reduction versus open reduction in the fixation of medial malleolar fractures. *Eur J Orthop Surg Traumatol* 2013; **23**: 953-959 [PMID: 23412228 DOI: 10.1007/s00590-012-1100-2]
- 14 **Castel H**, Bonneh DY, Sherf M, Liel Y. Awareness of osteoporosis and compliance with management guidelines in patients with newly diagnosed low-impact fractures. *Osteoporos Int* 2001; **12**: 559-564 [PMID: 11527053 DOI: 10.1007/s001980170077]
- 15 **Suarez-Almazor M**, Homik JE, Messina D, Davis P. Attitudes and beliefs of family physicians and gynecologists in relation to the prevention and treatment of osteoporosis. *J Bone Miner Res* 1997; **12**: 1100-1107 [PMID: 9200010 DOI: 10.1359/jbmr.1997.12.7.1100]
- 16 **Zhen D**, Liu L, Guan C, Zhao N, Tang X. High prevalence of vitamin D deficiency among middle-aged and elderly individuals in northwestern China: its relationship to osteoporosis and lifestyle factors. *Bone* 2015; **71**: 1-6 [PMID: 25284157 DOI: 10.1016/j.bone.2014.09.024]
- 17 **Smith JT**, Halim K, Palms DA, Okike K, Bluman EM, Chiodo CP. Prevalence of vitamin D deficiency in patients with foot and ankle injuries. *Foot Ankle Int* 2014; **35**: 8-13 [PMID: 24127268 DOI: 10.1177/1071100713509240]
- 18 **Lauritzen JB**, Lund B. Risk of hip fracture after osteoporosis fractures. 451 women with fracture of lumbar spine, olecranon, knee or ankle. *Acta Orthop Scand* 1993; **64**: 297-300 [PMID: 8322584 DOI: 10.3109/17453679308993629]
- 19 **Angthong C**, Angthong W, Harnroongroj T, Naito M, Harnroongroj T. Survival times of patients with a first hip fracture with and without subsequent major long-bone fractures. *J Nippon Med Sch* 2013; **80**: 42-49 [PMID: 23470805 DOI: 10.1272/jnms.80.42]

P- Reviewer: Nikolopoulos D **S- Editor:** Song XX **L- Editor:** A
E- Editor: Wu HL



Retrospective Study

Use of Ligament Advanced Reinforcement System tube in stabilization of proximal humeral endoprosthesis

Nikolaos A Stavropoulos, Hassan Sawan, Firas Dandachli, Robert E Turcotte

Nikolaos A Stavropoulos, Firas Dandachli, Robert E Turcotte, Department of Orthopedic Surgery, McGill University Health Centre, Montreal, QC H3G 1A4, Canada

Hassan Sawan, King Fahad Medical City, Riyadh 13521-7751, Saudi Arabia

Author contributions: Stavropoulos NA and Turcotte RE designed the study; Stavropoulos NA, Sawan H and Turcotte RE analysed the literature; Stavropoulos NA, Sawan H and Dandachli F acquired and analyzed the data; Turcotte RE supervised the project and critically reviewed the draft; all authors approved the final submitted version of the manuscript.

Institutional review board statement: We are pleased to inform you that request has been found ethically acceptable and we hereby grant you approval, *via* expedited review by the Chairman on August 9, 2013, to conduct the aforementioned study at the McGill University Health Centre.

Informed consent statement: As per our regulations no informed consent is required to perform a retrospective review analysis of medical records and X-rays. Personal informations were kept confidential.

Conflict-of-interest statement: All authors declare that they have no conflict of interest. No benefits of any source were received for the production of this work.

Data sharing statement: As per our regulations no data sharing statement is required to perform a retrospective review analysis of medical records and X-rays. Personal informations were kept confidential.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Robert E Turcotte, MD, FRCS(c), Chairman of the Department of Orthopaedic Surgery, McGill University Health Centre, 1650 Cedars Ave #B5 159.6, Montreal, QC H3G 1A4, Canada. robert.turcotte@muhc.mcgill.ca
Telephone: +1-514-9341934-42266
Fax: +1-514-9348453

Received: October 18, 2015
Peer-review started: October 20, 2015
First decision: December 7, 2015
Revised: January 11, 2016
Accepted: January 27, 2016
Article in press: January 29, 2016
Published online: April 18, 2016

Abstract

AIM: To review outcomes following usage of the Ligament Advanced Reinforcement System (LARS®) in shoulder tumors.

METHODS: Medical records of nineteen patients (19 shoulders) that underwent tumor excisional procedure and reconstruction with the LARS synthetic fabric, were retrospectively reviewed.

RESULTS: Patients' median age was 58 years old, while the median length of resection was 110 mm (range 60-210 mm). Compared to immediate post-operative radiographs, the prosthesis mean end-point position migrated superiorly at a mean follow up period of 26 mo ($P = 0.002$). No statistical significant correlations between the prosthesis head size ($P = 0.87$); the implant stem body length ($P = 0.949$); and the length of resection ($P = 0.125$) with the position of the head, were found at last follow up. Two cases of radiological dislocation were noted but only one was clinically symptomatic. A minor superficial wound dehiscence, healed without surgery, occurred. There was no

evidence of aseptic loosening either, and no prosthetic failure.

CONCLUSION: LARS[®] use ensured stability of the shoulder following endoprosthetic reconstruction in most patients.

Key words: Proximal humeral endoprotheses; Ligament Advanced Reinforcement System

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Endoprosthetic replacement of the proximal humerus for tumor resection offers predictable outcome. In an attempt to optimize functional scores, the use of Ligament Advanced Reinforcement System (LARS) tubes was facilitated. Our retrospective analysis revealed that LARS was not associated with specific complications. Its ability to ensure shoulder stability was good, albeit not perfect. Superior migration of the humeral head was common over time.

Stavropoulos NA, Sawan H, Dandachli F, Turcotte RE. Use of Ligament Advanced Reinforcement System tube in stabilization of proximal humeral endoprotheses. *World J Orthop* 2016; 7(4): 265-271 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i4/265.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i4.265>

INTRODUCTION

Latest advances in the diagnosis and management of neoplastic diseases, conferring prolonged life expectancy, have resulted in limb-salvage surgery as the main treatment choice for patients with bone and soft tissues sarcomas^[1-4]. Endoprotheses use has increased over the last 30 years with the overall 5-year survival rate rising from 20% to 85%^[1,3,5].

The upper extremity neoplasms are a third less common than lower extremity ones^[6]. Metastatic Bone Disease (MBD) is the most common cause of destructive bone lesions in adults, with the humerus as the second most common site, following the femur^[7-9]. The proximal humerus (PH) is also the third most common region for osteosarcoma^[6]. Even though limb-sparing surgery is the treatment of choice for 95% of tumors of the shoulder girdle, significant functional loss may follow^[10]. Since the first reported operation, a partial scapulectomy for an aneurysmal tumor of the subscapular artery performed by Liston^[11] in 1819, many surgical techniques have been described. Tumors of the PH should always meet the following values: (1) oncological principles of resection; (2) reconstruction of the missing segment; and (3) soft tissue reconstruction^[10]. The success of any technique is established upon the ability to achieve a long disease-free survival, and a stable and functional shoulder

joint. This may be impeded by complications such as aseptic or septic loosening, infection and mechanical failure^[11,12]. Recently, a new classification of these complications has been proposed with soft tissue and joint instability referred to as Type 1 failure^[13]. An unstable joint may lead to pain, discomfort, distress and inability to benefit from maximal usage of the hand and elbow. Stability relies primarily on the soft tissue envelope which includes: Labrum, joint capsule, rotator cuff and surrounding muscles. Maintaining joint stability can be rather challenging after the extensive resection of these structures, and albeit fundamental, ability to reattach soft tissues to the implant remains limited^[13-15]. Although various implant suspension methods using tapes, wires or tendons have been described^[16-21], the incidence of instability or dislocation has rarely been studied.

Capsuloplasty is achieved through reconstruction of the shoulder capsule with synthetic or collagenic tissue to secure stability. A previous study reported a 4.3% incidence of cranial subluxation of the proximal or total humerus prosthesis with synthetic Trevira[®] use^[2]. The Ligament Advanced Reinforcement System (LARS[®], Arc-sur-Tille, France), an artificial fabric made of polyethylene terephthalate, presents a great capacity for cellular and connective tissue properties both in the *in vitro* and *in vivo* studies^[22,23]. It has been used mainly for knee ligament augmentation or replacement^[24-27]. Our purpose was to report the results of the LARS[®] tube in the stabilization of proximal humeral endoprosthetic replacement for tumors, and to categorize any potential risk associated with its use.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 19 consecutive patients who underwent proximal humeral replacement, either due to sarcoma or to metastatic disease, followed by soft tissue reconstruction with LARS[®] synthetic fabric (LARS, Arc sur Tille, France). All procedures were performed by a single surgeon (RT). Implants were all Modular Replacement System of PH (MRS PH) (Stryker Orthopaedics Kalamazoo, Michigan, United States) (Figure 1). Extra articular resection was performed in one case only. Patients were operated through a standard deltopectoral approach with en bloc resection of the biopsy tract when applicable. According to the length of resection and soft tissue invasion, muscles and tendons were excised or detached from their bony attachment. Resection of the deltoid muscle may have differed based on the primary diagnosis. Joint capsule and rotator cuff tendons were sectioned at joint line level, and the labrum was preserved in all intra-articular resections. The axillary nerve was sacrificed in 2 cases. Surgical margins were assessed intraoperatively by pathologists. Reaming of the humeral medullary canal was performed and stem size was selected based on line to line sizing (French paradox)^[21,28]. Implants were selected with respect to the length of resection and the humeral head size,

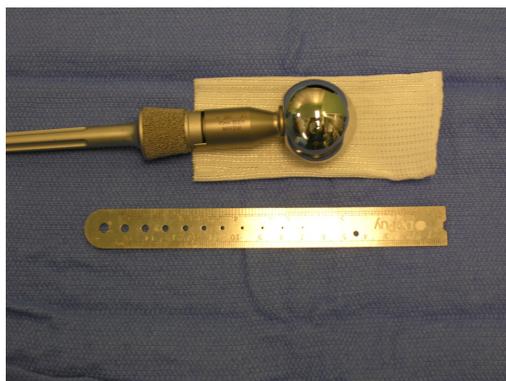


Figure 1 The prosthesis used was the Modular Replacement System of Proximal Humerus (Stryker Orthopaedics Kalamazoo, Michigan, United States).



Figure 2 Proper preparation of the Ligament Advanced Reinforcement System tubing that was cut the appropriate length to properly cover the head and body but short of covering the porous surface of the implant immediately adjacent to the host humerus.

Table 1 Classification of humerus head implant position

1	> 50% inferior migration of Prosthesis H.Head
2	< 50% inferior migration of Prosthesis H.Head
3	Centralized
4	< 50% superior migration of Prosthesis H.Head
5	> 50% superior migration of Prosthesis H.Head
6	Unstable

either 40 or 44 mm. Proper cementation of the definitive construct was then performed ensuring the expected 40-45 degrees of retroversion of the head. The LARS[®] tube was cut the appropriate length to properly cover the head and body but short of covering the porous surface of the implant immediately adjacent to the host humerus (Figure 2). The fabric was secured to the implant with #5 Ethibond[®] sutures. The proximal end of the tube fabric was spitted open allowing suturing to the remaining glenoid capsule and labrum in a circumferential manner figure of eight with #2 Ethibond[®] sutures (Figures 3 and 4). This usually led to an initial passive range of motion approximating 50 degrees of abduction and flexion and 40 degrees of internal and external rotation. No anchors were used. Shoulder stability was evaluated by pulling the arm longitudinally from the scapula and found stable in all directions. Severed tendons and muscles were reattached to the fabric with non resorbable sutures when possible. Postoperatively, the upper extremity was left into an arm and cuff sling for 6 wk, to allow for scarring, after which it was discarded. Active and passive ranging of the elbow and hand was encouraged right after surgery. Particular attention was paid to the stability of the implant and the existence of any identifiable adverse effect of the LARS fabric. Digitized radiographs were obtained with patient in standing position and without any arm support.

Two independent reviewers performed a double-blind evaluation of the Anteroposterior (AP) views of the digitized radiographs. An object of known size was used as a marker to identify any magnification error. In order to evaluate the position of the prosthesis and the

glenohumeral translation in the follow-up period, the percentage of the prosthesis head in correlation with the glenoid center, and with the superior and inferior glenoid rims, was assessed (Figure 5). The difference in distances between the midline from the glenoid center, and the midline from the center of the head of the prosthesis, was estimated and classified as shown in Table 1. Additionally, shoulder stability was evaluated by reviewing clinical notes. Functional assessment was based on the 1987 Musculoskeletal Tumor Society functional scoring system (MSTS)^[29] collected prospectively preoperatively and at 3, 6, 12, 24 and 36 mo after surgery^[29]. The analysis was performed by means of statistical software package (IBM SPSS v.19.0) statistical package. This study was approved by the hospital ethics committee. Study comprised 19 shoulders from 19 patients that underwent endoprosthetic replacement of the proximal humerus. Bone sarcoma made for 10 cases and metastatic disease for 9.

RESULTS

Ten patients were male. The median age was 58 years old (range: 23 to 77 years). Fifteen patients were right handed, three were left handed and one described himself as ambidextrous. Resection involved the right side in only 10 patients. Two thirds of cases (68%) presented with pathological fractures, and four patients had received neoadjuvant and adjuvant chemotherapy. Patients' characteristics are listed in Table 2. Following appropriate and individualized oncological pre-operative management, they underwent proximal humeral replacement and soft tissue reconstruction using the LARS synthetic fabric. The median length of resection was 110 mm (range 60-210 mm). The median humerus head size was 44 mm (range 35-50 mm), however, in 2 cases head size could not be measured due to the extent of bony destruction. In 9 patients the 40 mm modular head implant was selected and the rest received the 44 mm prosthesis. The implant body median length was 60 mm (range 40-140 mm). Utilizing the LARS

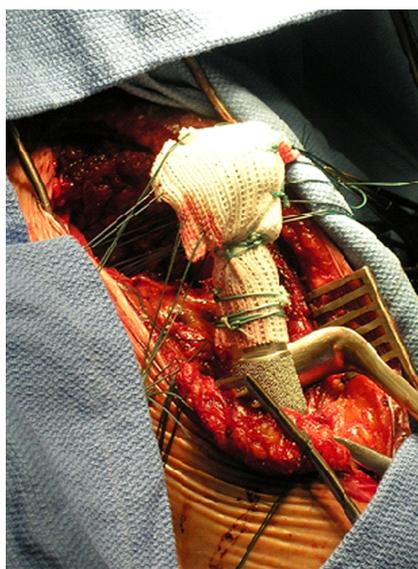


Figure 3 Suturing the remaining glenoid capsule and labrum with the proximal end of the fabric.

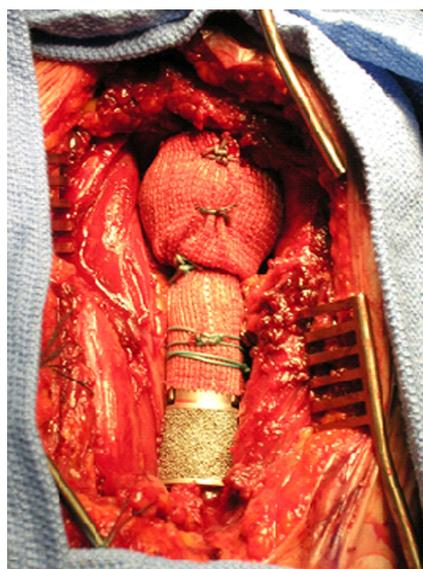


Figure 4 Final position of the proximal humeral endoprotheses.

Table 2 Patients characteristics				
Patient	Sex	Age	Diagnosis	Lesion side
1	Male	43	Ewing sarcoma	R
2	Male	58	Telangiectatic osteogenic sarcoma	R
3	Female	31	Chondrosarcoma	L
4	Female	53	Metastatic carcinoma renal cell primary	R
5	Male	67	Metastatic lung primary	L
6	Female	51	Metastatic lung primary adenocarcinoma	R
7	Male	64	Chondrosarcoma	L
8	Female	63	Metastatic thyroid	L
9	Female	52	Chondrosarcoma	R
10	Female	64	Metastatic clear cell renal	L
11	Male	23	Ewing sarcoma	R
12	Male	54	Metastatic renal cell carcinoma	L
13	Female	61	Metastatic breast	R
14	Male	70	Metastatic renal	L
15	Female	51	Metastatic undifferentiated sarcoma of bone	L
16	Female	68	Chondrosarcoma	L
17	Male	66	Metastatic clear cell renal	R
18	Male	77	Metastatic lung adenocarcinoma	R
19	Male	52	Multiple myeloma	R

L: Left; R: Right.

tube allowed the deltoid to be reattached in 9 patients and the pectoralis major and long head of the biceps (or what was left of it) in 8 patients. Primary closure was achieved for all patients with no need for flap mobilization. No significant neurological deficit affecting elbow and hand function was identified. No local recurrence was detected as per clinical examination and radiological evaluation. Although mechanical loosening was not found, one patient complained of discomfort relating to gross instability. No identifiable adverse local tissue reactions were noted and there was no sign of delayed wound healing, even in patients who had

undergone preoperative radiotherapy. A single case of minor superficial wound dehiscence, requiring minor care, occurred in the perioperative period. Radiological follow-up ranged from 14 to 2400 d (mean = 418 d). The overall follow-up period ranged from 14 to 2400 d (mean = 806 d).

Based on the proposed classification for head positioning with respect to the glenoid, statistical analysis revealed a mean post-operative starting position of 2.63 (from 3 = centralized head in the glenoid). The prosthesis mean final position was 3.68 (as 4 means < 50% superior migration). The prosthesis mean end-position tended to migrate more superiorly, at a mean follow up period of 26 mo ($P = 0.002$) (Figure 6). Inter observer reliability with respect to interpretation of the radiographs was very strong (kappa = 0.929 $P < 0.01$), thus, strength of agreement was almost perfect according to the Landis and Koch criteria^[30]. During the follow up period, 2 prostheses were considered radiographically dislocated, but only one was symptomatically unstable and dislocated, requiring further surgical stabilization. No statistical significant correlation was found between the head size of the prosthesis used ($P = 0.87$); the size of the implant stem body height ($P = 0.949$); the length of resection ($P = 0.125$), and the position of the head at last follow up.

The functional results were described based on the functional rating system of the Musculoskeletal Tumor Society and the Toronto Extremity Salvage Score (TESS)^[29,31,32]. Mean preoperative MSTs and TESS scores were 15.2 and 62.9, while the postoperative mean scores were 15.5 and 65 respectively. There was no correlation between preoperative MSTs score and end-function.

DISCUSSION

Endoprosthetic replacement of the PH offers a pre-

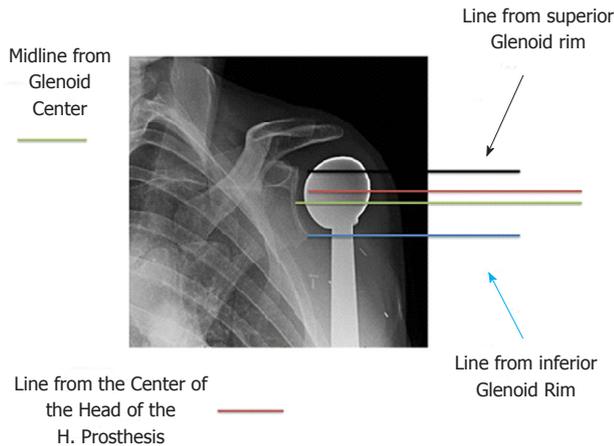


Figure 5 Radiological assessment of humerus head implant position.

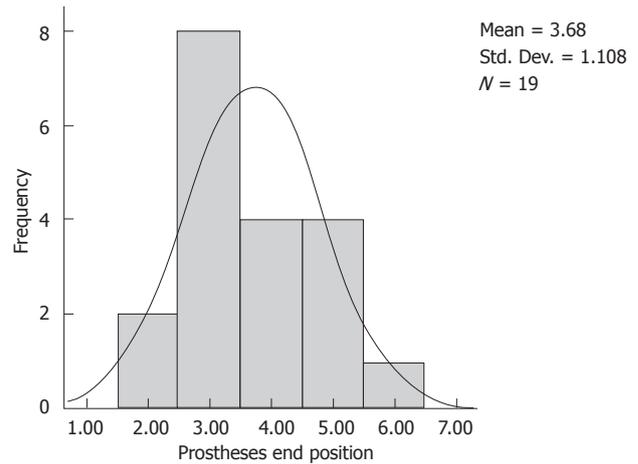


Figure 6 Prosthesis end position.

dictable outcome, with acceptable cosmetic and complication rates, albeit the functional results are limited by the lack of active mobility and strength. It is a durable construct however, stability remains a challenge.

Since the first endoprosthetic PH replacement by Pean in 1893, with a platinum and rubber alloy implant, many different procedures have been described^[33]. Sacrificing the rotator cuff and the deltoid in favor of oncological wider margins, and symptomatic instability with painful impingement on the subacromial arch, have been challenging potential complications^[15]. Several authors have advocated capsuloplasty, using a mesh-like fabric aiming at providing a more stable prosthesis by fixing the prosthesis to the glenoid, and allowing the reattachment of the surrounding muscles and tendons^[16,34,35]. Capsuloplasty, using Dacron aortic graft and Trevira Tubes, has been studied and reports support its usage^[34]. The common features that characterize these fabrics are biocompatibility and porosity that encourage tissue ingrowth, and strength that reduces shearing forces. By using Dacron aortic graft, authors have reported a decrease in symptomatic instability with no increase in infection or reoperation rates^[34]. Improvement of post-operative shoulder function was demonstrated and thought to be related to reattachment of the rotator cuff to Trevira tubes around the prosthesis^[36]. Histopathological examination of the soft tissue surrounding Trevira tubes revealed ingrowth of fibrous tissues and no foreign body granuloma or inflammatory process^[36]. LARS[®] was used to reconstruct soft tissue around four knees and three proximal femurs after tumor resection, and was found to be effective in improving stability and providing muscle attachment^[22].

Being a retrospective study and having a heterogenic small sample size of patients are among the few study weaknesses followed by the fact that there was not a control group of patients without LARS to compare with. We identified two cases with dislocation (10.4%), although only one was symptomatically unstable. Follow up period was relatively short and it is possible that further proximal migration of the implant may be noted after a longer follow up period. However, migration

tended to occur early on and then stabilized. Moreover, our classification proposal may have been thought to be among our study's weaknesses as it has never been described before. There was no other complication of significance including deep infection. Our works is among the few studies reporting about LARS for stabilization of proximal humeral prostheses. Some studies reported instability ranging between 0% and 11% using other types of fabric or techniques^[16,34,36]. A recent series of interscapulothoracic resection for shoulder tumors found no difference in stability whether LARS was used or not^[37]. Our study differs from others as we recorded progressive migration of the implant over time^[38]. We found that most implants migrated superiorly and anteriorly. Implants stable in their end position were found to be without measurable clinical effect. Our only symptomatic patient had gross instability on every attempt at active shoulder motion.

Our study, as others, supports the reconstruction of the shoulder capsule as an effective way of minimizing symptomatic instability. It is unclear which, if any material would be superior to another. It remains unclear in other studies if there was a progressive superior and anterior migration of the implant over time, but it certainly could not be prevented with the LARS[®] and the suturing technique utilized here. Nevertheless, it resulted in a stable construct in 18 of the 19 cases and provided adequate function of the elbow and hand. Even in cases when there may be some migration, the consequences for stability and overall function would be of minor clinical relevance.

COMMENTS

Background

Malignant tumors or metastasis of proximal humerus may cause significant loss of function. Endoprosthetic replacement is the most common way to reconstruct the resected bony part following limb salvage procedure, provide normal use of the hand and elbow and optimize the shoulder's postoperative functional outcome.

Research frontiers

Shoulder implant instability leads to pain, discomfort, and inability to benefit of the

functional outcomes of the procedure. Maintaining joint stability is challenging.

Innovations and breakthroughs

Use of the LARS® tube in the stabilization of proximal humeral endoprosthesis replacement for tumors and identification of any potential risk associated with its use.

Applications

Literature has advocated the use of various types of tissue, including synthetic or xenograft, to help reconstruct a new capsule over the proximal humeral endoprosthesis and maintain the proper positioning and stability. This retrospective analysis revealed that facilitation of LARS tubes in the endoprosthesis replacement of the proximal humerus was not associated with specific complications and proved to provide good, although not perfect, shoulder stability. Longer length of follow up would be needed to confirm that proximal and anterior migration does not progress.

Terminology

LARS is an abbreviation for Ligament Advanced Reinforcement System. TESS is an abbreviation for Toronto Extremity Salvage Score. MSTs is an abbreviation for Musculoskeletal Tumor Society Score.

Peer-review

This article is very good.

REFERENCES

- 1 **DiCaprio MR**, Friedlaender GE. Malignant bone tumors: limb sparing versus amputation. *J Am Acad Orthop Surg* 2003; **11**: 25-37 [PMID: 12699369]
- 2 **Gosheger G**, Gebert C, Ahrens H, Streitbuenger A, Winkelmann W, Harges J. Endoprosthesis reconstruction in 250 patients with sarcoma. *Clin Orthop Relat Res* 2006; **450**: 164-171 [PMID: 16691142 DOI: 10.1097/01.blo.0000223978.36831.39]
- 3 **Mittermayer F**, Krepler P, Dominkus M, Schwameis E, Sluga M, Heinzl H, Kotz R. Long-term followup of uncemented tumor endoprosthesis for the lower extremity. *Clin Orthop Relat Res* 2001; **(388)**: 167-177 [PMID: 11451116 DOI: 10.1097/00003086-200107000-00024]
- 4 **Sluga M**, Windhager R, Lang S, Heinzl H, Bielack S, Kotz R. Local and systemic control after ablative and limb sparing surgery in patients with osteosarcoma. *Clin Orthop Relat Res* 1999; **(388)**: 120-127 [PMID: 9973983 DOI: 10.1097/00003086-199901000-00015]
- 5 **Zeegen EN**, Aponte-Tinao LA, Hornicek FJ, Gebhardt MC, Mankin HJ. Survivorship analysis of 141 modular metallic endoprosthesis at early followup. *Clin Orthop Relat Res* 2004; **(420)**: 239-250 [PMID: 15057104 DOI: 10.1097/00003086-200403000-00034]
- 6 **Malawer MM**, Link M, Donaldson S. Sarcomas of bone. In: Devita VT, Hellman S, Rosenberg SA (ed). *Cancer: Principles and Practice of Oncology*, 3rd ed. JB Lippincott Philadelphia, 1984: 1418-1468
- 7 **Dijkstra S**, Stapert J, Boxma H, Wiggers T. Treatment of pathological fractures of the humeral shaft due to bone metastases: a comparison of intramedullary locking nail and plate osteosynthesis with adjunctive bone cement. *Eur J Surg Oncol* 1996; **22**: 621-626 [PMID: 9005151 DOI: 10.1016/S0748-7983(96)92450-6]
- 8 **Frassica FJ**, Frassica DA. Evaluation and treatment of metastases to the humerus. *Clin Orthop Relat Res* 2003; **(415 Suppl)**: S212-S218 [PMID: 14600613 DOI: 10.1097/01.blo.0000093052.96273.a7]
- 9 **Wedin R**, Hansen BH, Laitinen M, Trovik C, Zaikova O, Bergh P, Kalén A, Schwarz-Lausten G, Vult von Steyern F, Walloe A, Keller J, Weiss RJ. Complications and survival after surgical treatment of 214 metastatic lesions of the humerus. *J Shoulder Elbow Surg* 2012; **21**: 1049-1055 [PMID: 21982491 DOI: 10.1016/j.jse.2011.06.019]
- 10 **Malawer MM**, Wittig J. Overview of Resections around the Shoulder Girdle: Anatomy, Surgical Considerations and Classification. In: Malawer MM, Sugarbaker PH (ed). *Treatment of Sarcomas and Allied Diseases*. Musculoskeletal Cancer Surgery. Washington: Kluwer

- Academic Publishers Washington Cancer Institute, 2001: 179-201
- 11 **Liston R**. Ossified aneurysmal tumor of the subscapular artery. *Edw Med J* 1820; **16**: 66-70
- 12 **Donati D**, Zavatta M, Gozzi E, Giacomini S, Campanacci L, Mercuri M. Modular prosthetic replacement of the proximal femur after resection of a bone tumour a long-term follow-up. *J Bone Joint Surg Br* 2001; **83**: 1156-1160 [PMID: 11764431 DOI: 10.1302/0301-620x.83b8.12165]
- 13 **Henderson ER**, Groundland JS, Pala E, Dennis JA, Wooten R, Cheong D, Windhager R, Kotz RI, Mercuri M, Funovics PT, Hornicek FJ, Temple HT, Ruggieri P, Letson GD. Failure mode classification for tumor endoprosthesis: retrospective review of five institutions and a literature review. *J Bone Joint Surg Am* 2011; **93**: 418-429 [PMID: 21368074 DOI: 10.2106/JBJS.J.00834]
- 14 **Ayoub KS**, Fiorenza F, Grimer RJ, Tillman RM, Carter SR. Extensible endoprosthesis of the humerus after resection of bone tumours. *J Bone Joint Surg Br* 1999; **81**: 495-500 [PMID: 10872374 DOI: 10.1302/0301-620x.81b3.9178]
- 15 **Fuhrmann RA**, Roth A, Venbrocks RA. Salvage of the upper extremity in cases of tumorous destruction of the proximal humerus. *J Cancer Res Clin Oncol* 2000; **126**: 337-344 [PMID: 10870644 DOI: 10.1007/s004320050353]
- 16 **Asavamongkolkul A**, Eckardt JJ, Eilber FR, Dorey FJ, Ward WG, Kelly CM, Wirganowicz PZ, Kabo JM. Endoprosthesis reconstruction for malignant upper extremity tumors. *Clin Orthop Relat Res* 1999; **(360)**: 207-220 [PMID: 10101327 DOI: 10.1097/0003086-199903000-00025]
- 17 **Frassica FJ**, Chao EY, Shives TC, Sim FH. Resection of malignant bone tumors about the shoulder. A preliminary report of reconstruction with a new modular spacer. *Clin Orthop Relat Res* 1991; **(267)**: 57-64 [PMID: 2044293 DOI: 10.1097/00003086-199106000-00007]
- 18 **Kumar D**, Grimer RJ, Abudu A, Carter SR, Tillman RM. Endoprosthesis replacement of the proximal humerus. Long-term results. *J Bone Joint Surg Br* 2003; **85**: 717-722 [PMID: 12892196]
- 19 **O'Connor MI**, Sim FH, Chao EY. Limb salvage for neoplasms of the shoulder girdle. Intermediate reconstructive and functional results. *J Bone Joint Surg Am* 1996; **78**: 1872-1888 [PMID: 8986665 DOI: 10.1097/01241398-199705000-00061]
- 20 **Ritschl P**, Piza-Katzer H, Pechmann U, Kotz R. Refixation of muscular insertions after endoprosthesis replacement of the proximal humerus. *Arch Orthop Trauma Surg* 1989; **108**: 386-389 [PMID: 2619527 DOI: 10.1007/bf00932453]
- 21 **Sharma S**, Turcotte RE, Isler MH, Wong C. Experience with cemented large segment endoprosthesis for tumors. *Clin Orthop Relat Res* 2007; **459**: 54-59 [PMID: 17545759 DOI: 10.1097/blo.0b013e3180514c8e]
- 22 **Ji T**, Tang X, Guo W. The use of Ligament Advanced Reinforcement System (LARS) in limb salvage surgery: a pilot clinical study. *J Arthroplasty* 2013; **28**: 892-894 [PMID: 23507073 DOI: 10.1016/j.arth.2012.11.011]
- 23 **Trieb K**, Blahovec H, Brand G, Sabeti M, Dominkus M, Kotz R. In vivo and in vitro cellular ingrowth into a new generation of artificial ligaments. *Eur Surg Res* 2004; **36**: 148-151 [PMID: 15178903 DOI: 10.1159/000077256]
- 24 **Gao K**, Chen S, Wang L, Zhang W, Kang Y, Dong Q, Zhou H, Li L. Anterior cruciate ligament reconstruction with LARS artificial ligament: a multicenter study with 3- to 5-year follow-up. *Arthroscopy* 2010; **26**: 515-523 [PMID: 20362832 DOI: 10.1016/j.arthro.2010.02.001]
- 25 **Machotka Z**, Scarborough I, Duncan W, Kumar S, Perraton L. Anterior cruciate ligament repair with LARS (Ligament Advanced Reinforcement System): a systematic review. *Sports Med Arthrosc Rehabil Ther Technol* 2010; **2**: 29 [PMID: 21138589 DOI: 10.1186/1758-2555-2-29]
- 26 **Tiefenboeck TM**, Thurmaier E, Tiefenboeck MM, Ostermann RC, Joestl J, Winnisch M, Schurz M, Hajdu S, Hofbauer M. Clinical and functional outcome after anterior cruciate ligament reconstruction using the LARS™ system at a minimum follow-up of 10 years. *Knee* 2015; **22**: 565-568 [PMID: 26122668 DOI: 10.1016/j.knee.2015.06.003]

- 27 **Hamido F**, Al Harran H, Al Misfer AR, El Khadrawe T, Morsy MG, Talaat A, Elias A, Nagi A. Augmented short undersized hamstring tendon graft with LARS® artificial ligament versus four-strand hamstring tendon in anterior cruciate ligament reconstruction: preliminary results. *Orthop Traumatol Surg Res* 2015; **101**: 535-538 [PMID: 25998274 DOI: 10.1016/j.otsr.2015.01.021]
- 28 **Langlais F**, Belot N, Ropars M, Lambotte JC, Thomazeau H. The long-term results of press-fit cemented stems in total knee prostheses. *J Bone Joint Surg Br* 2006; **88**: 1022-1026 [PMID: 16877600]
- 29 **Enneking WF**. Modification of the System for Functional Evaluation in the Surgical Management of Musculoskeletal Tumors. In: Enneking WF (eds). *Limb Salvage in Musculoskeletal Oncology*. New York: Churchill Livingstone, 1987: 626-639
- 30 **Landis JR**, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; **33**: 159-174 [PMID: 843571 DOI: 10.2307/2529310]
- 31 **Davis AM**, Bell RS, Badley EM, Yoshida K, Williams JI. Evaluating functional outcome in patients with lower extremity sarcoma. *Clin Orthop Relat Res* 1999; **(358)**: 90-100 [PMID: 9973980 DOI: 10.1097/00003086-199901000-00012]
- 32 **Davis AM**, Wright JG, Williams JI, Bombardier C, Griffin A, Bell RS. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual Life Res* 1996; **5**: 508-516 [PMID: 8973131 DOI: 10.1007/bf00540024]
- 33 **Lugli T**. Artificial shoulder joint by Péan (1893): the facts of an exceptional intervention and the prosthetic method. *Clin Orthop Relat Res* 1978; **(133)**: 215-218 [PMID: 357063 DOI: 10.1097/0003086-197806000-00025]
- 34 **Marulanda GA**, Henderson E, Cheong D, Letson GD. Proximal and total humerus reconstruction with the use of an aortograft mesh. *Clin Orthop Relat Res* 2010; **468**: 2896-2903 [PMID: 20568029 DOI: 10.1007/s11999-010-1418-1]
- 35 **Wada T**, Usui M, Isu K, Yamawakii S, Ishii S. Reconstruction and limb salvage after resection for malignant bone tumour of the proximal humerus. A sling procedure using a free vascularised fibular graft. *J Bone Joint Surg Br* 1999; **81**: 808-813 [PMID: 10530841 DOI: 10.1302/0301-620x.81b5.9430]
- 36 **Gosheger G**, Hillmann A, Lindner N, Rödl R, Hoffmann C, Bürger H, Winkelmann W. Soft tissue reconstruction of megaprotheses using a trevira tube. *Clin Orthop Relat Res* 2001; **(393)**: 264-271 [PMID: 11764358 DOI: 10.1097/00003086-200112000-00030]
- 37 **Xie L**, X D T, Yang RL, Guo W. Interscapulothoracic resection of tumours of shoulder with a note on reconstruction. *Bone Joint J* 2014; **96-B**: 684-690 [PMID: 24788506 DOI: 10.1302/0301-620X.96B5.32241]
- 38 **Ji T**, Tang X, Guo W. Enhancing soft-tissue reattachment in proximal humeral endoprosthesis reconstruction. *J Orthop Surg (Hong Kong)* 2014; **22**: 100-103 [PMID: 24781625]

P- Reviewer: Garcia-Elorriaga G **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 May 18; 7(5): 272-342



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

Contents

Monthly Volume 7 Number 5 May 18, 2016

REVIEW

- 272 Management of metal-on-metal hip implant patients: Who, when and how to revise?
Berber R, Skinner JA, Hart AJ

MINIREVIEWS

- 280 Bernese periacetabular osteotomy for hip dysplasia: Surgical technique and indications
Kamath AF
- 287 Controversial role of arthroscopic meniscectomy of the knee: A review
Ha AY, Shalvoy RM, Voisinnet A, Racine J, Aaron RK
- 293 Resection and reconstruction of pelvic and extremity soft tissue sarcomas with major vascular involvement: Current concepts
McGoldrick NP, Butler JS, Lavelle M, Sheehan S, Dudeney S, O'Toole GC
- 301 Valgus osteotomy for nonunion and neglected neck of femur fractures
Varghese VD, Livingston A, Boopalan PR, Jpegnanam TS

ORIGINAL ARTICLE

Prospective Study

- 308 From Cape Town to Cambridge: Orthopaedic trauma in contrasting environments
Lawrence JE, Khanduja V

SYSTEMATIC REVIEWS

- 315 Management of lumbar zygapophysial (facet) joint pain
Manchikanti L, Hirsch JA, Falco FJE, Boswell MV

CASE REPORT

- 338 Methicillin-resistant *Staphylococcus aureus* infected gluteal compartment syndrome with rhabdomyolysis in a bodybuilder
Woon CYL, Patel KR, Goldberg BA

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Dr. Tsuyoshi Ohishi, MD, PhD, Department of Orthopedic Surgery, Hospital Enshu, Hamamatsu, Shizuoka 430-0929, Japan

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Su-Qing Liu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLICATION DATE
 May 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjgnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>

Management of metal-on-metal hip implant patients: Who, when and how to revise?

Reshid Berber, John A Skinner, Alister J Hart

Reshid Berber, John A Skinner, Alister J Hart, Joint Reconstruction Unit, Institute of Orthopaedics and Musculoskeletal Sciences, Royal National Orthopaedic Hospital, London HA7 4LP, United Kingdom

Author contributions: All listed authors were involved in the literature review and writing of this manuscript; all three authors contributed equally to this work.

Conflict-of-interest statement: The authors declare that they no conflict of interest; Skinner JA and Hart AJ have a consultancy agreement with Depuy and Stryker for metal on metal hip retrieval work.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Reshid Berber, MBBS, BSc (Hons), MRCS (Eng), Orthopaedic Registrar and Research Fellow, Joint Reconstruction Unit, Institute of Orthopaedics and Musculoskeletal Sciences, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, London HA7 4LP, United Kingdom. reshidb@gmail.com
Telephone: +44-20-89095621
Fax: +44-20-89095100

Received: July 29, 2015

Peer-review started: July 29, 2015

First decision: September 30, 2015

Revised: January 12, 2016

Accepted: March 7, 2016

Article in press: March 9, 2016

Published online: May 18, 2016

Abstract

The debate on how best to manage patients with metal-

on-metal (MOM) hip implants continues. With over 1 million patients affected worldwide, the impact is far reaching. The majority of the aggressive failures of MOM hip implants have been dealt with by revision hip surgery, leaving patients with a much more indolent pattern of failure of devices that have been *in situ* for more than 10 years. The longer-term outcome for such patients remains unknown, and much debate exists on how best to manage these patients. Regulatory guidance is available but remains open to interpretation due to the lack of current evidence and long-term studies. Metal ion thresholds for concern have been suggested at 7 ppb for hip resurfacing arthroplasty and below this level for large diameter total hip arthroplasties. Soft tissue changes including pseudotumours and muscle atrophy have been shown to progress, but this is not consistent. New advanced imaging techniques are helping to diagnose complications with metal hips and the reasons for failure, however these are not widely available. This has led to some centres to tackle difficult cases through multidisciplinary collaboration, for both surgical management decisions and also follow-up decisions. We summarise current evidence and consider who is at risk, when revision should be undertaken and how patients should be managed.

Key words: Metal on metal hip; Management; Multi-disciplinary; Revision; Decision

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Evidence supporting the management of metal on metal hips is lacking, and guidance is open to interpretation. Until supporting evidence is available, an evidence based multi-disciplinary approach on a case-by-case basis is considered a safe method to help surgeons make decisions and potentially improve patient outcomes.

Berber R, Skinner JA, Hart AJ. Management of metal-on-metal

hip implant patients: Who, when and how to revise? *World J Orthop* 2016; 7(5): 272-279 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/272.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.272>

INTRODUCTION

Considerable debate continues to surround the use and management of patients with failing metal-on-metal (MOM) hip implants. Over a million patients worldwide have been implanted with a MOM device^[1], and according to the United Kingdom National Joint Registry (NJR), their use peaked in 2006 [hip resurfacing arthroplasty (HRA)] and 2008 [large diameter total hip replacement (LDTHR)]^[2]. However, due to several concerns of catastrophic soft tissue reactions leading to early failures and associated complications, medical device alerts were published^[3], and MOM hips were subsequently withdrawn from use by the British Hip Society in 2012.

It is clear that there are evolving and changing patterns of behaviour in the failure of MOM hips^[4]. Many of the early, aggressive failures have been dealt with by revision hip surgery, and we now see a much more indolent pattern of failure in patients who have had devices *in situ* for more than 10 years.

This spectrum of patients from the well functioning, that require only monitoring, to the poorly functioning, which require revision continues to evoke debate among surgeons, especially since the bulk of patients fall between these two extremes Figures 1 and 2. Uncertainties surround thresholds for investigation, revision surgery and methods for surveillance^[5]. Guidance from international regulatory agencies exists, but tend to reflect the needs of local health authorities, which accounts for some of the variation seen in the guidance^[3,6,7].

This review examines the literature on current clinical dilemmas facing surgeons and their patients with MOM hip replacements, and summarises current clinical guidance for how and when patients should be managed.

MOM hip implants

MOM hip implants consist of two broad types, the HRA and the LDTHR. Since their inception in 1937^[4], they have gone through several key design changes and modifications, with the expected fluctuations in their use. Their use flourished in the 1990s with the introduction of the modern HRA and subsequently accounted for approximately a third of all hip replacements being implanted in the United States in 2008^[1].

The proposed benefits for using MOM bearings were to reduce the occurrence of polyethylene disease (aseptic loosening) and to allow the use of large diameter femoral head components to reduce the occurrence of hip dislocation^[4]. However, the inception of highly cross-linked polyethylene and improved ceramic bearing

design, have diminished the perceived advantages of MOM over other bearing surfaces^[8,9].

Besides this, metal debris and corrosion products have led to inflammatory reactions within the soft tissues surrounding MOM hip implants and subsequently their early failure and need for revision^[10-13]. This has led to the subsequent fall in use of MOM hips and intervention from regulators^[3].

Metal debris - A cause for concern?

Metal implants are considered biologically inert, however wear debris is not and is thought to evoke an immune response^[14]. The release of material from metallic implants occurs by wear, corrosion and mechanical factors such as fretting and third body wear. Cobalt and chromium are the major constituents of alloy metal implants, and are the main cause for concern.

Metal particulate and ionic wear debris from the hip is released into the peri-prosthetic tissues and transported systemically throughout the body^[15,16]. Studies have demonstrated a peak in blood cobalt levels at 6-mo post implantation and chromium levels at 9-mo, followed by a steady decline over time^[17,18]. Following revision of a MOM implant to an alternative bearing, blood ion levels reduce but do not normalise in the post-operative period^[19,20].

Component design and positioning has been shown to be associated with increased wear and as a result raised metal ion levels^[21-25]. Blood cobalt and chromium ion levels in patients with unexplained painful MOM hips are double those of well-functioning MOM hips^[13].

Wear debris can accumulate locally as seen by studies of joint fluid surrounding MOM hip implants^[26-28]. The level of chromium is greater in joint fluid compared to cobalt, whereas the converse is true for blood analysis^[28]. However it is believed that cobalt is the species with greatest reactivity causing local tissue inflammatory reactions due to its ready solubility^[29-31].

WHO IS AT RISK?

Local soft tissue reactions

Pseudotumours are well described in patients with MOM hip implants, and can be either solid or cystic. Reported prevalence in both symptomatic and asymptomatic patients ranges from 0.1% to 69%^[10,11,32-37]. The precise aetiology is not known, however the term aseptic lymphocytic vasculitis-associated lesion (ALVAL) is used to describe the histological features associated with metal hips^[38]. It has been suggested that a delayed type IV hypersensitivity reaction to metal ions is the potential cause, however this has been challenged^[12]. Pseudotumours were, however, shown to correlate with elevated blood and hip aspirate metal ion levels suggesting a relation to excessive implant wear^[12,39].

Recent evidence regarding the natural history of soft tissues abnormalities is conflicting. Studies report varying degrees of progression in size and grade of pseudotumours, however limitations in sample size,

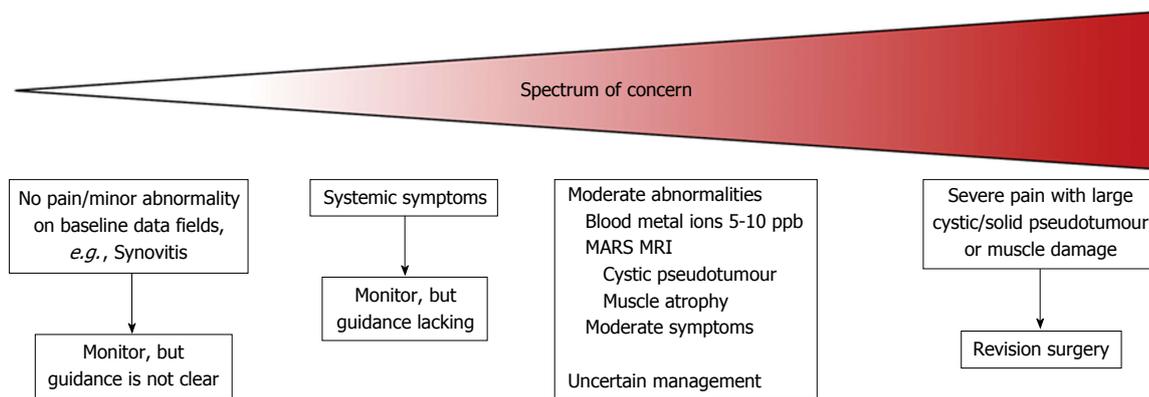


Figure 1 Diagram demonstrating the spectrum of concern for patients with metal-on-metal hip implants. The decision on how to manage patients at the extremes of the spectrum is relatively straightforward. However the majority of patients fall into to the middle category, where the management is uncertain or difficult. MRI: Magnetic resonance imaging; MARS: Metal artefact reduction sequence.

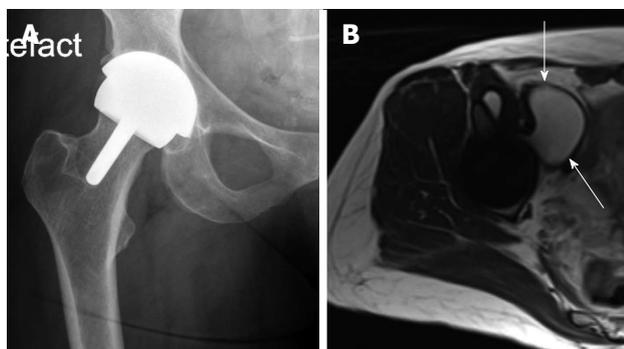


Figure 2 Middle of the spectrum - A typical patient with moderate problems. This 58-year-old very active lady with a right hip resurfacing arthroplasty (A: X-ray AP hip) implanted 8 years ago. She has minimal symptoms and moderately raised blood metal ion levels (Cobalt 13 ppb, Chromium 7 ppb). A magnetic resonance imaging scan (B: Axial T2 weighted image) has revealed a 6 cm cystic pseudotumour anterior to the hip (arrows).

implant type and imaging modality do not readily allow the generalisability of the results^[40-42]. It appears that when disease progression does occur, it is slow and therefore serial imaging annually is sufficient to identify change. The potential to cause local pressure effects causing necrosis and compression of nearby structures such as the iliac vessels, femoral vessels and the sciatic nerve is also a concern.

Muscle atrophy is now becoming an increasing concern, and is driving the debate regarding the timing of revision surgery in order to prevent irreversible damage. A recent publication demonstrated progressive muscle atrophy using serial magnetic resonance imaging (MRI) scanning in a mixed cohort of patients^[43].

Systemic effects

Several cases of systemic effects from metal hip implants have been reported, including cardiac, endocrine, neurological and dermatological complications, however this remains a relatively rare occurrence^[44]. There is a mixture of cases reported in both fractured ceramic hips and in primary MOM hip patients^[44]. Removal of the implant led to reduced metal ion levels and symptomatic

improvement in several of these cases. Additionally, chronic low dose exposure over several years revealed a negative effect on cardiac function and bone density^[45], however these were subtle and sub-clinical. Recent cases of cardiac toxicity have been further highlighted and novel diagnostic techniques are being explored^[46,47].

MANAGEMENT - WHEN SHOULD PATIENTS BE REVISED?

The local and systemic effects of metal particulate and ionic debris from MOM hips have led to increased rates of revision hip surgery. It has also led to significant levels of patient anxiety, not to mention the physical and financial burden of a failed metal implant on the patient and the health services.

The British Hip Society was the first to publish their guidance through the Medicines and Healthcare Products Regulatory Agency (MHRA)^[3]. The MOM task force (American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons, and The Hip Society) in the United States^[48], the European Hip Society (EHS) (2012)^[6], and most recently the European Commission’s Scientific Committee on Emerging and Newly Identified Health Risks, have also published guidance for surgeons^[49]. However, uncertainties remain over decision making because of the difficulty - for any guideline - to define or quantify clinical symptoms, imaging findings and clinically important thresholds for blood metal ion results.

Role of metal ions

The MHRA currently recommends 7 ppb as the threshold for concern beyond which further investigations are recommended to diagnose complications associated with MOM hip implants. The Food and Drug Administration (FDA) does not currently set an action level, and SCENIHR acknowledge that the level for concern lies between 2-7 ppb based on questions raised regarding the current available evidence.

The population background level of cobalt in blood

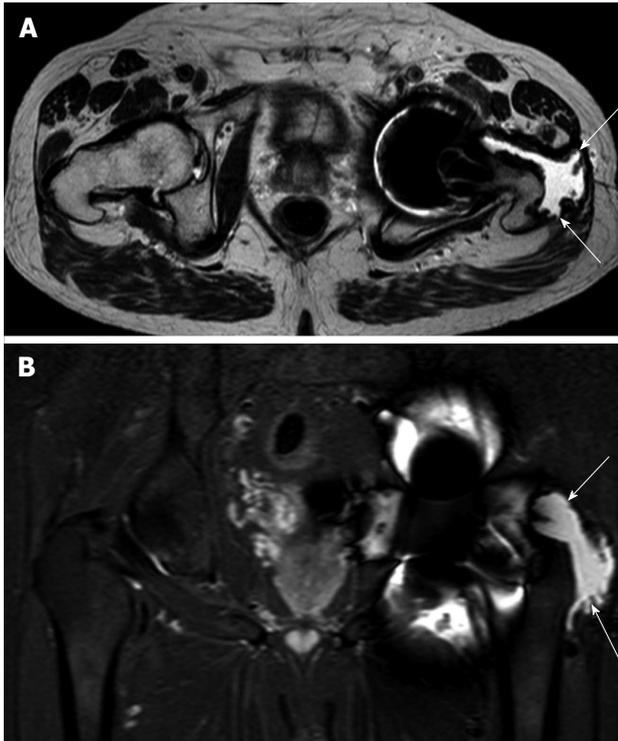


Figure 3 Axial (A) and coronal (B) magnetic resonance imaging. Example of abductor stripping secondary to a pseudotumour (marked by arrows). The pseudotumour can be seen traversing the posterior hip around the greater tuberosity onto its lateral aspect, which is now void of abductor tendon insertion.

has been shown to be 0.5 ppb. There is a correlation seen with wear rates, where 2 ppb can be expected with wear rates of 2 cubic mm per year^[50,51].

Since the 7 ppb level was derived from research based on hip resurfacings^[51], it has been postulated that this may not apply to stemmed implants. A study including a variety of implant types demonstrated improved sensitivity and specificity with a threshold cobalt level of 4.5 ppb^[50].

Various groups have argued for a blood metal ion threshold for revision. The prevalence of patients with blood metal ion levels over 25 ppb was 2.6% in HRA patients, and 3.1% in total Hip Replacement (THR) patients^[52]. The sensitivity and specificity of the 7 ppb cut-off level have been reported to be 52% and 89%, respectively, indicating that the 7 ppb has relative poor ability to identify MOM failures. The lowering of the cut-off level to 5 ppb increases the sensitivity to 63% and lowers specificity to 86%^[51]. The Finland group demonstrated that 25 ppb was 99% specific compared to 93% specificity at 7 ppb, however more notably revised patients with metal ions over 25 ppb had a significantly lower oxford hip score 12 mo after revision compared to those with ions less than 25 ppb. The re-revision rate was also higher in those patients with metal ions over 25 ppb^[52].

Based on current literature 7 ppb remains a safe level for concern in patients with a HRA implant, whereas the presence of a taper (LDTHR) would prompt a lower

threshold for concern.

Role of diagnostic imaging

The MHRA advise metal artefact reduction sequence MRI (MARS MRI) or ultrasound scan as part of the investigation algorithm^[3]. MARS MRI appears more appropriate, due to excellent sensitivity and specificity for detection of both superficial and deep lesions^[53-55], and also muscle atrophy. Ultrasound is a satisfactory modality for identifying tendon abnormalities^[54]. Current MARS MRI techniques do suffer from metal artefact that limits the diagnosis of osteolysis, however, improved techniques are being developed^[56]. Currently computed tomography (CT) scanning is ideal for visualising osteolysis if it is suspected on plain radiographs^[57].

In patients where the cause of pain is unexplained, single-photon emission CT (SPECT-CT) has been recommended^[58]. SPECT-CT was shown to be clinically valuable in diagnosing the cause of pain and influenced management decisions in over half of patients with unexplained pain following a MOM hip arthroplasty despite inconclusive conventional investigations.

Pseudotumours

There is a lack of evidence surrounding the need for revision secondary to pseudotumours, particularly regarding the outcome following revision surgery and the long-term natural history of pseudotumours. This is reflected in the current guidance by the limited detail in how to interpret MRI findings.

It has been shown that revision for pseudotumour is associated with significant post-operative complications^[59]. In addition, recurrence after revision with excision is possible and may be as high as 30%. If pseudotumours, cystic or solid, are large enough to cause pressure necrosis or stretch of soft tissues, then this is usually an indication for revision surgery (Figure 3).

Large pseudotumours with intra-pelvic extensions along the psoas sheath or arising wholly within the pelvis are of particular concern. These have the potential for compression of neurovascular structures including the iliac vessels. In addition, surgical excision becomes more difficult and often a multi-disciplinary surgical approach with vascular surgeons is required (Figure 4).

Osteolysis

Osteolysis surrounding MOM hip implants is a further concern that needs to be addressed^[60], and one should be vigilant in the presence of very high metal ions. Progressive osteolysis may be an indication for early intervention if the potential for peri-prosthetic fracture is apparent.

Muscle atrophy

There is growing evidence supporting early revision to a non-MOM hip implant to prevent irreversible damage^[38,61]. Campbell *et al*^[62] observed that patients can expect a good outcome if their soft tissues remain

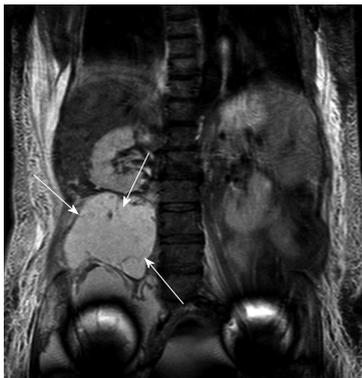


Figure 4 A 58-year-old patient with bilateral large diameter total hip replacement metal-on-metal implanted 9-years ago, moderate hip symptoms and raised metal ion levels (Cobalt 17 ppb, Chromium 13 ppb). She presented to the general surgeons with abdominal pain and distension. Coronal magnetic resonance imaging scan (above) demonstrated a large cystic pseudotumour extending into the pelvis up to the level of the L2 vertebra and abutting the right kidney in the retroperitoneal space (arrows). The cystic pseudotumour was drained prior to surgical excision with both orthopaedic and vascular surgeons present.

intact. A recent study demonstrated progressive muscle atrophy over a period of 12 mo using serial MRI, and noted an association with high metal ion levels^[43]. Liddle *et al*^[63] highlight the degree of misdiagnosis possible when planning for revision of MOM hip implants. They describe that pre-operative imaging can underestimate the degree of soft tissue abnormalities seen at revision surgery including a high rate of severe abductor muscle atrophy and stripping of the tendinous attachment^[63]. If progressive and destructive soft tissue change is possible, predicting those patients that are likely to fail is paramount so that revision can be undertaken early to ensure a better outcome (Figure 3).

Broadly however, a decision to revise should not be based on a single investigation, instead the decision should take into account patient symptoms, activity level, implant type, metal ion levels and imaging findings.

WHEN SHOULD PATIENTS BE FOLLOWED UP?

Current guidance stratifies patients by risk depending on the type of implant they have *in situ*. Small diameter THR and hip resurfacing arthroplasty is considered low risk, whereas the large diameter THR and the DePuy ASR implants are considered high risk^[3]. A recent publication went one step further and stratified all current generation MOM hip implants into low, medium and high risk categories^[5], based on registry and regulatory advice. More recently however the Regulators state that low risk implants that are functioning well should be monitored according to local hospital protocols, whereas high-risk implants require follow-up for the life of the implant. The Birmingham Hip Resurfacing (Smith and Nephew, London, United Kingdom) has been the best performing hip resurfacing, however concerns have always existed regarding their

use in female patients, and patients with small diameter femoral heads (< 48 mm). As a result of these concerns the MHRA have released further guidance advising against their use in this population and additional advice on the management of patients with these implants *in situ*^[64].

However the majority of guidelines do not offer detail on what constitutes follow up, and more importantly which patients require more frequent monitoring. A pragmatic approach would be to take this on a case-by-case basis where the frequency of follow up needs to be tailored to the individual based on the implant risk stratification and the patients clinical status.

Based on the literature, with particular reference to the natural history of soft tissue changes, annual follow up would suffice for those with a medium to high risk implant. Follow up should consist of a history, clinical examination, functional scoring, blood metal ions measurement and X-ray. If clinical concern exists then cross sectional imaging with MARS MRI would be indicated. For low risk implants in individuals with a low risk profile, then less intensive follow-up would be indicated, such as annual questionnaires and 5-yearly clinical review.

One must be mindful of applying a simplistic approach based on implant risk stratification alone, since certain aspects of the patients clinical and surgical history would suggest a heightened risk even in the best performing hip implants. Low risk implants in patients with hip symptoms, evidence of soft tissue abnormality or high metal ions would require closer monitoring. In addition, excessive acetabular cup inclination can lead to edge loading and early failure^[65,66], and also female patients with small femoral head size hip resurfacing arthroplasties and females with primary hip dysplasia have worse long term outcomes^[48].

HOW - MULTI-DISCIPLINARY TEAM APPROACH

Some clinical cases are straightforward and decision-making is relatively easy. However, in many instances surgeons experience considerable uncertainty in decision-making because of the lack of guidelines or the difficulty in applying guidelines in complex cases. This gap has led to the use of a multidisciplinary teams (MDT) approach to help interpret the guidance published by the regulatory agencies, with the aim of using surgical experience, tacit knowledge, and evidence-based current best practice to reduce the uncertainty surrounding the management of patients with MOM hip implants^[5].

This highlights the need for a more collaborative approach between surgeons, regulators and industry representatives to improve the available evidence and the guidance offered to aid the management of patients with MOM hip implants.

Role of retrievals

In a recent commentary by Jacobs *et al*^[67], the im-

portance of implant retrieval analysis by centres with access to large retrieval cohorts was emphasized as significant in understanding mechanisms of failure and also for developing future preclinical testing models. This reflects the number of developments established through retrieval analysis and includes the relationship with cup position and edge loading^[68], the correlation of wear rates with blood metal ion levels^[66] and the role of frictional torque and fretting currents in LDTHR^[69].

CONCLUSION

The management of patients with MOM hip implants continues to cause concern and difficulties for patients and surgeons alike. The evidence is lacking in certain scenarios, and regulatory guidance can be interpreted differently. When considering which patient requires revision, no single investigation or aspect of the history should be taken in isolation. Decisions should be taken on a case-by-case basis, with consideration given to all aspects of the patient's clinical history and investigation results. A multi-disciplinary approach with shared decision-making, tacit knowledge and surgical experience appears to be a safe and practical approach to improving patient's outcomes.

REFERENCES

- 1 **Bozic KJ**, Kurtz S, Lau E, Ong K, Chiu V, Vail TP, Rubash HE, Berry DJ. The epidemiology of bearing surface usage in total hip arthroplasty in the United States. *J Bone Joint Surg Am* 2009; **91**: 1614-1620 [PMID: 19571083 DOI: 10.2106/JBJS.H.01220]
- 2 **Borrorff M**, Green M, Gregg P, MacGregor A, Porter M, Tucker K, Wishart N. 11th Annual Report 2014 - National Joint Registry for England, Wales and Northern Ireland. 2014
- 3 **Ludgate S**, Haque F, Cacou C. Medical Device Alert: All metal-on-metal (MoM) hip replacements. [Updated 2012 Aug 9]. Available from: URL: <http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con155767.pdf>
- 4 **Haddad FS**, Thakrar RR, Hart AJ, Skinner JA, Nargol AV, Nolan JF, Gill HS, Murray DW, Blom AW, Case CP. Metal-on-metal bearings: the evidence so far. *J Bone Joint Surg Br* 2011; **93**: 572-579 [PMID: 21511920 DOI: 10.1302/0301-620X.93B4.26429]
- 5 **Berber R**, Pappas Y, Khoo M, Miles J, Carrington R, Skinner J, Hart A. A new approach to managing patients with problematic metal hip implants: the use of an Internet-enhanced multidisciplinary team meeting: AAOS exhibit selection. *J Bone Joint Surg Am* 2015; **97**: e20 [PMID: 25695991 DOI: 10.2106/JBJS.N.00973]
- 6 **Hannemann F**, Hartmann A, Schmitt J, Lützner J, Seidler A, Campbell P, Delaunay CP, Drexler H, Ettema HB, Garcia-Cimbrello E, Huberti H, Knahr K, Kunze J, Langton DJ, Lauer W, Learmonth I, Lohmann CH, Morlock M, Wimmer MA, Zagra L, Günther KP. European multidisciplinary consensus statement on the use and monitoring of metal-on-metal bearings for total hip replacement and hip resurfacing. *Orthop Traumatol Surg Res* 2013; **99**: 263-271 [PMID: 23507457 DOI: 10.1016/j.otsr.2013.01.005]
- 7 **Food and Drug Administration U**. Metal-on-Metal Hip Implants - Advice for Surgeons. [Updated 2014 May 10]. Available from: URL: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/MetalonMetalHipImplants/ucm241667.htm>
- 8 **Hart AJ**, Sabah SA, Henckel J, Lloyd G, Skinner JA. Lessons learnt from metal-on-metal hip arthroplasties will lead to safer innovation for all medical devices. *Hip Int* 2015; **25**: 347-354 [PMID: 26165359 DOI: 10.5301/hipint.5000275]
- 9 **Graves S**, Davidson D, de Steiger R, Lewis P, Stoney J. Annual Report 2014 - Australian orthopaedic association national joint replacement registry. 2014
- 10 **Pandit H**, Glyn-Jones S, McLardy-Smith P, Gundle R, Whitwell D, Gibbons CL, Ostlere S, Athanasou N, Gill HS, Murray DW. Pseudotumours associated with metal-on-metal hip resurfacings. *J Bone Joint Surg Br* 2008; **90**: 847-851 [PMID: 18591590 DOI: 10.1302/0301-620X.90B7.20213]
- 11 **Kwon YM**, Ostlere SJ, McLardy-Smith P, Athanasou NA, Gill HS, Murray DW. "Asymptomatic" pseudotumors after metal-on-metal hip resurfacing arthroplasty: prevalence and metal ion study. *J Arthroplasty* 2011; **26**: 511-518 [PMID: 20591612 DOI: 10.1016/j.arth.2010.05.030]
- 12 **Kwon YM**, Thomas P, Summer B, Pandit H, Taylor A, Beard D, Murray DW, Gill HS. Lymphocyte proliferation responses in patients with pseudotumors following metal-on-metal hip resurfacing arthroplasty. *J Orthop Res* 2010; **28**: 444-450 [PMID: 19834954 DOI: 10.1002/jor.21015]
- 13 **Hart AJ**, Sabah S, Henckel J, Lewis A, Cobb J, Sampson B, Mitchell A, Skinner JA. The painful metal-on-metal hip resurfacing. *J Bone Joint Surg Br* 2009; **91**: 738-744 [PMID: 19483225 DOI: 10.1302/0301-620X.91B6.21682]
- 14 **Wooley PH**, Nasser S, Fitzgerald RH. The immune response to implant materials in humans. *Clin Orthop Relat Res* 1996; **(326)**: 63-70 [PMID: 8620660]
- 15 **Case CP**, Langkamer VG, James C, Palmer MR, Kemp AJ, Heap PF, Solomon L. Widespread dissemination of metal debris from implants. *J Bone Joint Surg Br* 1994; **76**: 701-712 [PMID: 8083255]
- 16 **Merritt K**, Brown SA. Release of hexavalent chromium from corrosion of stainless steel and cobalt-chromium alloys. *J Biomed Mater Res* 1995; **29**: 627-633 [PMID: 7622548]
- 17 **Daniel J**, Ziaee H, Pradhan C, McMinn DJ. Six-year results of a prospective study of metal ion levels in young patients with metal-on-metal hip resurfacings. *J Bone Joint Surg Br* 2009; **91**: 176-179 [PMID: 19190049 DOI: 10.1302/0301-620X.91B2.21654]
- 18 **Jacobs JJ**, Skipor AK, Campbell PA, Hallab NJ, Urban RM, Amstutz HC. Can metal levels be used to monitor metal-on-metal hip arthroplasties? *J Arthroplasty* 2004; **19**: 59-65 [PMID: 15578555 DOI: 10.1016/j.arth.2004.09.019]
- 19 **Ball ST**, Severns D, Linn M, Meyer RS, Swenson FC. What happens to serum metal ion levels after a metal-on-metal bearing is removed? *J Arthroplasty* 2013; **28**: 53-55 [PMID: 23948123 DOI: 10.1016/j.arth.2013.06.040]
- 20 **Ebreo D**, Khan A, El-Meligy M, Armstrong C, Peter V. Metal ion levels decrease after revision for metallosis arising from large-diameter metal-on-metal hip arthroplasty. *Acta Orthop Belg* 2011; **77**: 777-781 [PMID: 22308623]
- 21 **De Haan R**, Pattyn C, Gill HS, Murray DW, Campbell PA, De Smet K. Correlation between inclination of the acetabular component and metal ion levels in metal-on-metal hip resurfacing replacement. *J Bone Joint Surg Br* 2008; **90**: 1291-1297 [PMID: 18827237 DOI: 10.1302/0301-620X.90B10.20533]
- 22 **Langton DJ**, Sprowson AP, Joyce TJ, Reed M, Carluke I, Partington P, Nargol AV. Blood metal ion concentrations after hip resurfacing arthroplasty: a comparative study of articular surface replacement and Birmingham Hip Resurfacing arthroplasties. *J Bone Joint Surg Br* 2009; **91**: 1287-1295 [PMID: 19794161 DOI: 10.1302/0301-620X.91B10.22308]
- 23 **Langton DJ**, Jameson SS, Joyce TJ, Webb J, Nargol AV. The effect of component size and orientation on the concentrations of metal ions after resurfacing arthroplasty of the hip. *J Bone Joint Surg Br* 2008; **90**: 1143-1151 [PMID: 18757952 DOI: 10.1302/0301-620X.90B9.20785]
- 24 **Hart AJ**, Skinner JA, Henckel J, Sampson B, Gordon F. Insufficient acetabular version increases blood metal ion levels after metal-on-metal hip resurfacing. *Clin Orthop Relat Res* 2011; **469**: 2590-2597 [PMID: 21656317 DOI: 10.1007/s11999-011-1930-y]
- 25 **Matthies AK**, Henckel J, Cro S, Suarez A, Noble PC, Skinner J, Hart AJ. Predicting wear and blood metal ion levels in metal-on-

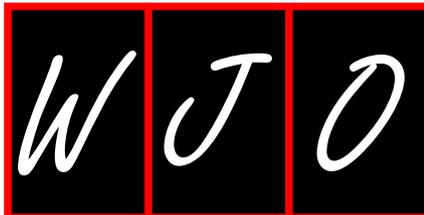
- metal hip resurfacing. *J Orthop Res* 2014; **32**: 167-174 [PMID: 24115200 DOI: 10.1002/jor.22459]
- 26 **De Smet K**, De Haan R, Calistri A, Campbell PA, Ebramzadeh E, Pattyn C, Gill HS. Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing. *J Bone Joint Surg Am* 2008; **90** Suppl 4: 202-208 [PMID: 18984732 DOI: 10.2106/JBJS.H.00672]
- 27 **Langton DJ**, Jameson SS, Joyce TJ, Hallab NJ, Natu S, Nargol AV. Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement: A consequence of excess wear. *J Bone Joint Surg Br* 2010; **92**: 38-46 [PMID: 20044676 DOI: 10.1302/0301-620X.92B1.22770]
- 28 **Davda K**, Lali FV, Sampson B, Skinner JA, Hart AJ. An analysis of metal ion levels in the joint fluid of symptomatic patients with metal-on-metal hip replacements. *J Bone Joint Surg Br* 2011; **93**: 738-745 [PMID: 21586770 DOI: 10.1302/0301-620X.93B6.25804]
- 29 **Hart AJ**, Quinn PD, Lali F, Sampson B, Skinner JA, Powell JJ, Nolan J, Tucker K, Donell S, Flanagan A, Mosselmans JF. Cobalt from metal-on-metal hip replacements may be the clinically relevant active agent responsible for periprosthetic tissue reactions. *Acta Biomater* 2012; **8**: 3865-3873 [PMID: 22688088 DOI: 10.1016/j.actbio.2012.05.003]
- 30 **Hart AJ**, Quinn PD, Sampson B, Sandison A, Atkinson KD, Skinner JA, Powell JJ, Mosselmans JF. The chemical form of metallic debris in tissues surrounding metal-on-metal hips with unexplained failure. *Acta Biomater* 2010; **6**: 4439-4446 [PMID: 20541630 DOI: 10.1016/j.actbio.2010.06.006]
- 31 **Goode AE**, Perkins JM, Sandison A, Karunakaran C, Cheng H, Wall D, Skinner JA, Hart AJ, Porter AE, McComb DW, Ryan MP. Chemical speciation of nanoparticles surrounding metal-on-metal hips. *Chem Commun (Camb)* 2012; **48**: 8335-8337 [PMID: 22801350 DOI: 10.1039/c2cc33016d]
- 32 **Canadian Hip Resurfacing Study Group**. A survey on the prevalence of pseudotumors with metal-on-metal hip resurfacing in Canadian academic centers. *J Bone Joint Surg Am* 2011; **93** Suppl 2: 118-121 [PMID: 21543700 DOI: 10.2106/JBJS.J.01848]
- 33 **Sabah SA**, Mitchell AW, Henckel J, Sandison A, Skinner JA, Hart AJ. Magnetic resonance imaging findings in painful metal-on-metal hips: a prospective study. *J Arthroplasty* 2011; **26**: 71-76, 76.e1-2 [PMID: 20149575 DOI: 10.1016/j.arth.2009.11.008]
- 34 **Williams DH**, Greidanus NV, Masri BA, Duncan CP, Garbuz DS. Prevalence of pseudotumor in asymptomatic patients after metal-on-metal hip arthroplasty. *J Bone Joint Surg Am* 2011; **93**: 2164-2171 [PMID: 22159851 DOI: 10.2106/JBJS.J.01884]
- 35 **Matthies AK**, Skinner JA, Osmani H, Henckel J, Hart AJ. Pseudotumors are common in well-positioned low-wearing metal-on-metal hips. *Clin Orthop Relat Res* 2012; **470**: 1895-1906 [PMID: 22179978 DOI: 10.1007/s11999-011-2201-7]
- 36 **Hart AJ**, Satchithananda K, Liddle AD, Sabah SA, McRobbie D, Henckel J, Cobb JP, Skinner JA, Mitchell AW. Pseudotumors in association with well-functioning metal-on-metal hip prostheses: a case-control study using three-dimensional computed tomography and magnetic resonance imaging. *J Bone Joint Surg Am* 2012; **94**: 317-325 [PMID: 22336970 DOI: 10.2106/JBJS.J.01508]
- 37 **Chang EY**, McAnally JL, Van Horne JR, Statum S, Wolfson T, Gamst A, Chung CB. Metal-on-metal total hip arthroplasty: do symptoms correlate with MR imaging findings? *Radiology* 2012; **265**: 848-857 [PMID: 23047842 DOI: 10.1148/radiol.12120852]
- 38 **Willert HG**, Buchhorn GH, Fayyazi A, Flury R, Windler M, Köster G, Lohmann CH. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. *J Bone Joint Surg Am* 2005; **87**: 28-36 [PMID: 15637030]
- 39 **Bosker BH**, Eetema HB, Boomsma MF, Kollen BJ, Maas M, Verheyen CC. High incidence of pseudotumor formation after large-diameter metal-on-metal total hip replacement: a prospective cohort study. *J Bone Joint Surg Br* 2012; **94**: 755-761 [PMID: 22628588 DOI: 10.1302/0301-620X.94B6.28373]
- 40 **Almoussa SA**, Greidanus NV, Masri BA, Duncan CP, Garbuz DS. The natural history of inflammatory pseudotumors in asymptomatic patients after metal-on-metal hip arthroplasty. *Clin Orthop Relat Res* 2013; **471**: 3814-3821 [PMID: 23536176 DOI: 10.1007/s11999-013-2944-4]
- 41 **Ebreo D**, Bell PJ, Arshad H, Donell ST, Toms A, Nolan JF. Serial magnetic resonance imaging of metal-on-metal total hip replacements. Follow-up of a cohort of 28 mm Ultima TPS THR. *Bone Joint J* 2013; **95-B**: 1035-1039 [PMID: 23908416 DOI: 10.1302/0301-620X.95B8.31377]
- 42 **van der Weegen W**, Brakel K, Horn RJ, Hoekstra HJ, Sijbesma T, Pilot P, Nelissen RG. Asymptomatic pseudotumours after metal-on-metal hip resurfacing show little change within one year. *Bone Joint J* 2013; **95-B**: 1626-1631 [PMID: 24293591 DOI: 10.1302/0301-620X.95B12.32248]
- 43 **Berber R**, Khoo M, Cook E, Guppy A, Hua J, Miles J, Carrington R, Skinner J, Hart A. Muscle atrophy and metal-on-metal hip implants: a serial MRI study of 74 hips. *Acta Orthop* 2015; **86**: 351-357 [PMID: 25588091 DOI: 10.3109/17453674.2015.1006981]
- 44 **Bradberry SM**, Wilkinson JM, Ferner RE. Systemic toxicity related to metal hip prostheses. *Clin Toxicol (Phila)* 2014; **52**: 837-847 [PMID: 25132471 DOI: 10.3109/15563650.2014.944977]
- 45 **Prentice JR**, Clark MJ, Hoggard N, Morton AC, Tooth C, Paley MN, Stockley I, Hadjivassiliou M, Wilkinson JM. Metal-on-metal hip prostheses and systemic health: a cross-sectional association study 8 years after implantation. *PLoS One* 2013; **8**: e66186 [PMID: 23762480 DOI: 10.1371/journal.pone.0066186]
- 46 **Khan AH**, Verma R, Bajpai A, Mackey-Bojack S. Unusual case of congestive heart failure: cardiac magnetic resonance imaging and histopathologic findings in cobalt cardiomyopathy. *Circ Cardiovasc Imaging* 2015; **8**: pii: e003352 [PMID: 26022382 DOI: 10.1161/CIRCIMAGING.115.003352]
- 47 **Samar HY**, Doyle M, Williams RB, Yamrozik JA, Bunker M, Biederman RW, Shah MB. Novel Use of Cardiac Magnetic Resonance Imaging for the Diagnosis of Cobalt Cardiomyopathy. *JACC Cardiovasc Imaging* 2015; **8**: 1231-1232 [PMID: 25797125 DOI: 10.1016/j.jcmg.2014.12.016]
- 48 **Kwon YM**, Lombardi AV, Jacobs JJ, Fehring TK, Lewis CG, Cabanela ME. Risk stratification algorithm for management of patients with metal-on-metal hip arthroplasty: consensus statement of the American Association of Hip and Knee Surgeons, the American Academy of Orthopaedic Surgeons, and the Hip Society. *J Bone Joint Surg Am* 2014; **96**: e4 [PMID: 24382732 DOI: 10.2106/JBJS.M.00160]
- 49 **Epstein M**, Emri I, Hartemann P, Hoet P, Leitgeb N, Martinez L, Proykova A, Rizzo L, Rodriguez-Farre E, Rushton L, Rydzynski K, Samaras T, Testai E, Vermeire T, Case C, Dekant W, De Jong W, Gunther K, Hensten A, Morlock M, Stea S, Van Der Straeten C, Verheyen C. The safety of Metal-on-Metal joint replacements with a particular focus on hip implants. [Updated 2014 Oct 14]. Available from: URL: http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_042.pdf
- 50 **Sidaginamale RP**, Joyce TJ, Lord JK, Jefferson R, Blain PG, Nargol AV, Langton DJ. Blood metal ion testing is an effective-screening tool to identify poorly performing metal-on-metal bearingsurfaces. *Bone Joint Res* 2013; **2**: 84-95 [PMID: 23836464 DOI: 10.1302/2046-3758.25.2000148]
- 51 **Hart AJ**, Sabah SA, Bandi AS, Maggiore P, Tarassoli P, Sampson B, A Skinner J. Sensitivity and specificity of blood cobalt and chromium metal ions for predicting failure of metal-on-metal hip replacement. *J Bone Joint Surg Br* 2011; **93**: 1308-1313 [PMID: 21969427 DOI: 10.1302/0301-620X.93B10.26249]
- 52 **Hart AJ**, Sabah SA, Sampson B, Skinner JA, Powell JJ, Palla L, Pajamäki KJ, Puolakka T, Reito A, Eskelinen A. Surveillance of Patients with Metal-on-Metal Hip Resurfacing and Total Hip Prostheses: A Prospective Cohort Study to Investigate the Relationship Between Blood Metal Ion Levels and Implant Failure. *J Bone Joint Surg Am* 2014; **96**: 1091-1099 [PMID: 24990974]
- 53 **Nawabi DH**, Hayter CL, Su EP, Koff MF, Perino G, Gold SL, Koch KM, Potter HG. Magnetic resonance imaging findings in symptomatic versus asymptomatic subjects following metal-on-metal hip resurfacing arthroplasty. *J Bone Joint Surg Am* 2013; **95**:

- 895-902 [PMID: 23677356 DOI: 10.2106/JBJS.K.01476]
- 54 **Siddiqui IA**, Sabah SA, Satchithananda K, Lim AK, Cro S, Henckel J, Skinner JA, Hart AJ. A comparison of the diagnostic accuracy of MARS MRI and ultrasound of the painful metal-on-metal hip arthroplasty. *Acta Orthop* 2014; **85**: 375-382 [PMID: 24694273 DOI: 10.3109/17453674.2014.908345]
- 55 **Garbuz DS**, Hargreaves BA, Duncan CP, Masri BA, Wilson DR, Forster BB. The John Charnley Award: Diagnostic accuracy of MRI versus ultrasound for detecting pseudotumors in asymptomatic metal-on-metal THA. *Clin Orthop Relat Res* 2014; **472**: 417-423 [PMID: 23868425 DOI: 10.1007/s11999-013-3181-6]
- 56 **Hayter CL**, Koff MF, Shah P, Koch KM, Miller TT, Potter HG. MRI after arthroplasty: comparison of MAVRIC and conventional fast spin-echo techniques. *AJR Am J Roentgenol* 2011; **197**: W405-W411 [PMID: 21862766 DOI: 10.2214/AJR.11.6659]
- 57 **Robinson E**, Henckel J, Sabah S, Satchithananda K, Skinner J, Hart A. Cross-sectional imaging of metal-on-metal hip arthroplasties. Can we substitute MARS MRI with CT? *Acta Orthop* 2014; **85**: 577-584 [PMID: 25267500 DOI: 10.3109/17453674.2014.964618]
- 58 **Berber R**, Henckel J, Khoo M, Wan S, Hua J, Skinner J, Hart A. Clinical Usefulness of SPECT-CT in Patients with an Unexplained Pain in Metal on Metal (MOM) Total Hip Arthroplasty. *J Arthroplasty* 2015; **30**: 687-694 [PMID: 25583682 DOI: 10.1016/j.arth.2014.11.019]
- 59 **Grammatopoulos G**, Pandit H, Kwon YM, Gundle R, McLardy-Smith P, Beard DJ, Murray DW, Gill HS. Hip resurfacings revised for inflammatory pseudotumour have a poor outcome. *J Bone Joint Surg Br* 2009; **91**: 1019-1024 [PMID: 19651827 DOI: 10.1302/0301-620X.91B8.22562]
- 60 **Randelli F**, Banci L, Favilla S, Maglione D, Aliprandi A. Radiographically undetectable periprosthetic osteolysis with ASR implants: the implication of blood metal ions. *J Arthroplasty* 2013; **28**: 1259-1264 [PMID: 23528557 DOI: 10.1016/j.arth.2013.02.019]
- 61 **Daniel J**, Holland J, Quigley L, Sprague S, Bhandari M. Pseudotumors associated with total hip arthroplasty. *J Bone Joint Surg Am* 2012; **94**: 86-93 [PMID: 22218386 DOI: 10.2106/JBJS.J.01612]
- 62 **Campbell P**, Shimmin A, Walter L, Solomon M. Metal sensitivity as a cause of groin pain in metal-on-metal hip resurfacing. *J Arthroplasty* 2008; **23**: 1080-1085 [PMID: 18534479 DOI: 10.1016/j.arth.2007.09.024]
- 63 **Liddle AD**, Satchithananda K, Henckel J, Sabah SA, Vipulendran KV, Lewis A, Skinner JA, Mitchell AW, Hart AJ. Revision of metal-on-metal hip arthroplasty in a tertiary center: a prospective study of 39 hips with between 1 and 4 years of follow-up. *Acta Orthop* 2013; **84**: 237-245 [PMID: 23621810 DOI: 10.3109/17453674.2013.797313]
- 64 **Medicines and Healthcare products Regulatory Agency**. Metal-on-metal (MoM) hip replacements - guidance on implantation and patient management MHRA 2015. [Accessed 2016 Jan 5]. Available from: URL: <http://www.gov.uk/drug-device-alerts/metal-on-metal-mom-hip-replacements-guidance-on-implantation-and-patient-management>
- 65 **Hart AJ**, Ilo K, Underwood R, Cann P, Henckel J, Lewis A, Cobb J, Skinner J. The relationship between the angle of version and rate of wear of retrieved metal-on-metal resurfacings: a prospective, CT-based study. *J Bone Joint Surg Br* 2011; **93**: 315-320 [PMID: 21357951 DOI: 10.1302/0301-620X.93B3.25545]
- 66 **Hart AJ**, Muirhead-Allwood S, Porter M, Matthies A, Ilo K, Maggiore P, Underwood R, Cann P, Cobb J, Skinner JA. Which factors determine the wear rate of large-diameter metal-on-metal hip replacements? Multivariate analysis of two hundred and seventy-six components. *J Bone Joint Surg Am* 2013; **95**: 678-685 [PMID: 23595065 DOI: 10.2106/JBJS.J.01447]
- 67 **Jacobs JJ**, Wimmer MA. An important contribution to our understanding of the performance of the current generation of metal-on-metal hip replacements. *J Bone Joint Surg Am* 2013; **95**: e53 [PMID: 23595079 DOI: 10.2106/JBJS.M.00137]
- 68 **Underwood RJ**, Zografos A, Sayles RS, Hart A, Cann P. Edge loading in metal-on-metal hips: low clearance is a new risk factor. *Proc Inst Mech Eng H* 2012; **226**: 217-226 [PMID: 22558836 DOI: 10.1177/0954411911431397]
- 69 **Panagiotidou A**, Meswania J, Osman K, Bolland B, Latham J, Skinner J, Haddad FS, Hart A, Blunn G. The effect of frictional torque and bending moment on corrosion at the taper interface : an in vitro study. *Bone Joint J* 2015; **97-B**: 463-472 [PMID: 25820883 DOI: 10.1302/0301-620X.97B4.34800]

P- Reviewer: Agilli M, Luo XH **S- Editor:** Qiu S

L- Editor: A **E- Editor:** Liu SQ





Bernese periacetabular osteotomy for hip dysplasia: Surgical technique and indications

Atul F Kamath

Atul F Kamath, Department of Orthopedic Surgery, Center for Hip Preservation, Pennsylvania Hospital, Philadelphia, PA 19107, United States

Author contributions: Kamath AF solely contributed to this paper.

Conflict-of-interest statement: The author has no conflicts of interest to disclose pertaining to the subject of this review manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Atul F Kamath, MD, Department of Orthopedic Surgery, Center for Hip Preservation, Pennsylvania Hospital, 800 Spruce Street, 8th Floor Preston, Philadelphia, PA 19107, United States. akamath@post.harvard.edu
Telephone: +1-215-6878169
Fax: +1-215-8292492

Received: May 24, 2015

Peer-review started: May 25, 2015

First decision: October 8, 2015

Revised: December 20, 2015

Accepted: February 14, 2016

Article in press: February 16, 2016

Published online: May 18, 2016

Abstract

For young, active patients with healthy hip cartilage, pelvic osteotomy is a surgical option in to address hip pain and to improve mechanical loading conditions related to dysplasia. Hip dysplasia may lead to arthrosis at an early age due to poor coverage of the femoral

head and abnormal loading of the joint articulation. In patients with symptomatic dysplasia and closed triradiate cartilage (generally over age 10), including adolescents and young adults (generally up to around age 40), the Bernese periacetabular osteotomy (PAO) is a durable technique for addressing underlying structural deformity. The PAO involves a modified Smith-Petersen approach. Advantages of the Bernese osteotomy include preservation of the weight-bearing posterior column of the hemi-pelvis, preservation of the acetabular blood supply, maintenance of the hip abductor musculature, and the ability to effect powerful deformity correction about an ideal center of rotation. There is an increasing body of evidence that preservation of the native hip can be improved through pelvic osteotomy. In contrast to hip osteotomy and joint preservation, the role of total hip arthroplasty in young, active patients with correctable hip deformity remains controversial. Moreover, the durability of hip replacement in young patients is inherently limited. Pelvic osteotomy should be considered the preferred method to address correctable structural deformity of the hip in the young, active patient with developmental dysplasia. The Bernese PAO is technically demanding, yet offers reproducible results with good long-term survivorship in carefully selected patients with preserved cartilage and the ability to meet the demands of rehabilitation.

Key words: Periacetabular osteotomy; Hip dysplasia; Pelvis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The periacetabular osteotomy has been used to address structural deformity in young patients with acetabular dysplasia. The technique through a modified Smith-Petersen approach offers advantages: Preservation of the posterior column adds to the stability of the hemipelvis and protection of the sciatic nerve, preservation of the acetabular blood supply, and

maintenance of hip abductor musculature. The juxta-articular osteotomy planes offer the ability to effect powerful deformity correction about an ideal center of rotation. While maximizing joint stability, coverage and congruency, the acetabular reorientation must also be assessed in light of the impingement-free range of motion.

Kamath AF. Bernese periacetabular osteotomy for hip dysplasia: Surgical technique and indications. *World J Orthop* 2016; 7(5): 280-286 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/280.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.280>

INTRODUCTION

The goal of pelvic osteotomy in the setting of hip dysplasia is to address the biomechanical and structural abnormalities that lead to secondary osteoarthritis under improper loading conditions. Poor coverage and/or incongruity due to developmental hip dysplasia may be corrected through reorientation of the acetabulum into an ideal position^[1]. By improving these loading conditions, the static and dynamic instability patterns seen with hip dysplasia can be appropriately countered. While reorienting the osteotomy fragment and increasing the femoral head coverage improve load distributions across the joint, the amount and direction of correction required depends on the individual patient. This correction remains the critical - and certainly the most challenging - part of the procedure.

Prior to surgery, a thorough history and physical examination is required, including a careful assessment of gait, leg lengths, joint stability, and range of motion. High-quality radiographs should be obtained. These studies include an anteroposterior pelvis projection in proper rotation and tilt, a Dunn lateral view of the hip (e.g., 45-degree projection), and a false profile (faux profile) view of the affected hemipelvis^[2]. To estimate the ability for containment and the amount of correction and resulting congruency possible with reorientation of the acetabulum, a functional abduction and internal rotation radiograph should be obtained as well. The patient's age, body mass index, level of activity, and functional goals must also be incorporated into a decision to pursue surgical intervention.

The Bernese, or Ganz, periacetabular osteotomy (PAO) is the author's preferred method for correcting acetabular dysplasia. Other pelvic osteotomies (e.g., triple, rotational) vary in the nature of the osteotomy planes, the ability to address open vs closed triradiate cartilage, and ability to correct acetabular orientation in multiple planes. The most frequent indication for performing the Bernese PAO is symptomatic acetabular dysplasia in an adolescent or young adult^[3] with correctable deformity and preserved range of motion. The procedure is generally performed after closure of the

triradiate cartilage (generally after age 10). Older patients (into the fourth decade) may be suitable candidates for the procedure based on the degree of arthrosis, as well as other factors such as ability to cope with rehabilitation period, activity level, expectations, obesity, and systemic conditions.

Contraindications to the Bernese PAO include advanced arthrosis (e.g., Tönnis Grade 2 or 3), subluxation resulting in a femoral head within a neoacetabulum, and a mismatch between a smaller acetabular radius and that of the femoral head which may cause worsening of joint congruity after reorientation. Patients with severe restrictions in range of motion are also poor surgical candidates.

SURGICAL TECHNIQUE

Equipment

An epidural catheter is placed pre-operatively and is continued post-operatively for pain control. Either regional anesthesia (e.g., spinal/epidural) vs general anesthesia with selective muscle relaxation may be used. General anesthesia may be performed with total intravenous anesthesia to maintain the ability to perform neuromonitoring during key exposure and reduction maneuvers that might put neurologic structures at highest risk. A Foley urinary catheter is also placed at the time of surgery. The patient is positioned supine on a radiolucent operating room table.

A fluoroscopy machine with a wide field of view may be used during the case for accurate and safe osteotomy cuts. A portable X-ray machine for obtaining intra-operative radiographs of the entire pelvis after acetabular correction is essential. Neuromonitoring during the case^[4] is optional but advised to ensure safe dissection and osteotomy maneuvers. A cell-salvage system is used to collect intra-operative blood loss, and tranexamic acid is routinely dosed prior to incision and during wound closure. A foot rest for stabilizing the limb in a position of hip flexion is attached to the operating table, or, alternatively, a radiolucent triangle or specialized sterile leg holder may be used to achieve hip flexion throughout the majority of the procedure.

Specialized PAO retractors, osteotomes (including Ganz-type osteotomes), and surgical instruments may be obtained through commercial sets (e.g., manufactured by Subtilis/Smith and Nephew). Steinman pins and Kirschner wires (including 1/8th, 5/64th, 3/32nd diameters), as well as Schanz screws (5.0 mm, 6.0 mm) with appropriate T-handle adaptors for intra-operative reduction maneuvers should be available. Likewise, a ball-spike pusher and bone-holding forceps/clamps, including Weber-type (e.g., as found on Synthes Pelvic Reduction instrument tray) are important for fragment reduction and fixation. Long 3.5 mm/4.5 mm screws and appropriate length depth gauge, drill bits, bone taps (as found on a Synthes Large Fragment and/or Pelvic Reconstruction set) are needed for fixation. Reconstruction plates may be used if poor bone quality

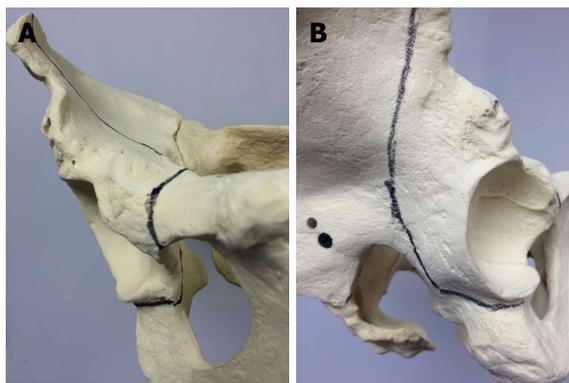


Figure 1 Location of osteotomy planes in the bernese periacetabular osteotomy. Frontal (A) and lateral (B) views of the pelvis demonstrating placement of juxta-acetabular osteotome cuts (dark lines).

is encountered or if there is a very large correction performed. Wide and narrow oscillating saw blades are used for osteotomy cuts, and a high-speed bur is used for acetabuloplasty and/or osteochondroplasty. Bone wax, drains (e.g., medium Hemovac), and heavy non-absorbable suture for tendinous repair are other miscellaneous equipment needed during the procedure.

Other equipment that should be available, but necessarily open for the start of the case, includes appropriate femoral osteotomy plating system, if performing concurrent femoral osteotomy; and acetabular labral suture anchors, with appropriate drilling system, for labral repair if indicated. Similarly, hip arthroscopy equipment and viewing tower should be available if a concomitant hip arthroscopy procedure is preferred over capsulotomy.

Patient positioning and draping

The patient is placed in the supine position on a radiolucent table. The ipsilateral upper limb may be placed across the chest, and all bony prominences are well-padded. Fluoroscopic views (antero-posterior pelvis and roll-over oblique) should be confirmed prior to definitive prep and draping of the limb. Access to above the level of the iliac crest of the operative hemipelvis and down to the ipsilateral foot must be included within the prepped field. Neuromonitoring leads may be secured to the involved extremity before final sterile draping.

Surgical exposure

The modified Smith-Petersen approach, with preservation of the abductor musculature, is utilized. A curvilinear skin incision, centered about the anterior superior iliac spine (ASIS) is used. This incision extends proximally along the iliac crest and distally along the internervous interval of the tensor fascia lata and sartorius muscles. The fascia over the tensor is incised along the orientation of the muscle fibers. The lateral femoral cutaneous nerve is protected proximally about the ASIS, as well as during distal superficial exposure. The tensor fascial muscle belly is separated from the fascial envelope bluntly and retracted laterally; slight

abduction may make this separation easier. Maintenance of this fascial sleeve also helps to protect the cutaneous nerve.

The ASIS is then osteotomized (block or wafer). This osteotomy maintains the origins of the sartorius and ilioinguinal ligament in continuity with the mobile fragment. The external oblique is dissected off the iliac wing in a subperiosteal plane for access to the inner pelvis down to the pelvic brim. The periosteum is elevated along with the iliacus muscle using straight and angled long Cobb-type elevators. If bleeding is encountered from the iliolumbar artery as it penetrates the iliac crest, the arterial orifice may be enlarged and then filled with bone wax.

The deep distal exposure is completed by reflecting the rectus tendon from the anterior inferior iliac spine, preserving a bed of tendon for later repair. As the deep fascia is opened distally, the pedicle to the tensor is exposed. This pedicle is freed, mobilized, and preserved. By dissecting the iliocapsularis muscle off the anterior hip capsule, an interval is developed medially under the iliopsoas tendon. The hip should be flexed up on a radiolucent triangle (or rested upon a foot bump) at this time to relax the anterior soft tissues. Completion of the dissection between the iliocapsularis, especially at its inferolateral border, allows the surgeon to palpate the calcar femoris through the capsule as well as the anterior surface of the ischium using closed scissors. Medial dissection exposes the iliopectineal bursa. Further subperiosteal exposure of the quadrilateral surface and pubic root allows for placement of a sharp Hohmann into the pubis, medial to the iliopectineal eminence.

Periacetabular osteotomies

The location of the various periacetabular osteotomy cuts are shown in Figure 1. Exposing the hip capsule inferiorly, the ischium is palpated with scissors. The ischium is triangular in shape with the base posterior. The infracotyloid groove, along with the obturator foramen medially and hamstrings origin laterally, is appreciated. The tips of the long curved dissecting scissors should be kept proximal to the obturator externus muscle. This scissor trajectory then guides the placement of a specialized curved osteotome to create the osteotomy just distal to the infracotyloid groove. The osteotome may be slid behind the scissors to ensure no entrapment of soft tissues. The position of the osteotome may be verified in anteroposterior and oblique fluoroscopic projections.

The inferior retro-acetabular osteotomy begins at the infracotyloid groove and progresses toward the midpoint of the ischial spine. The osteotomy is done in both medial and lateral limbs: The osteotomy is begun on the medial side. During the lateral osteotomy, the sciatic nerve should be relaxed with the limb abducted, the hip extended, and the knee in slight flexion. Both tactile and aural feedback is critical in assuring the osteotome is within bone, as well as to prevent violation

of the posterior column. The ischial osteotomy is an incomplete osteotomy, with depth to about 2.5 cm. It is important to cut the thicker medial cortex, while the thinner lateral cortex may break in a controlled fashion during the final osteotomy expansion maneuvers.

An assistant may then adduct the hip (maintaining flexion) to aid in access to the pubic ramus. The ramus periosteum is sharply cut on the superior cortical surface, and square-tip retractors are placed around the postero-inferior and postero-superior aspects of the pubic ramus. These retractors encircle the bone and protect the obturator nerve. Adequate circumferential release of the periosteum must be ensured to allow later fragment mobility, especially in younger patients with thick periosteum. A spiked Hohmann is secured into the superior cortex of the ramus a couple centimeters medial to the medial border of the iliopectineal eminence. This safely retracts the iliopsoas and the femoral neurovascular bundle medially, while maintaining a safe distance from the joint. A thin-kerf narrow saw (may alternatively use an osteotome) is used to start the osteotomy at an angle away from the joint; the osteotomy is completed with an osteotome. Removing a thin wafer of bone from the anterior cortex may help with sounding the far posterior cortex. The posterior cortex cut should exit medial to the obturator nerve. An osteotome may be used to gently splay the osteotomy to ensure that the cut is complete.

The ischial spine is identified with a reverse Eva retractor placed on the inside of the ischial spine after subperiosteal presentation of the quadrilateral surface. A muscular window along the lateral surface of the iliac wing is created, and a second reverse Eva is placed laterally. This tunnel along the outer table protects the gluteal muscles. The level of this iliac osteotomy is at a sufficient distance from the acetabulum to minimize risk of injury to the superior gluteal artery (supra-acetabular branch) and vascular arcade supplying the acetabulum. Furthermore, a larger bone bridge allows for better purchase of the Schanz screw during reduction, as well as to minimize the chance of joint surface violation while performing the second limb of the retro-acetabular cuts. A burr is used to make a target hole approximately 1 cm superolateral to the brim of the true pelvis. Alternatively, an osteotome may be used to mark this eventual vertex of the 120-degree osteotomy limbs. The osteotomy of the ilium is started with an oscillating saw: The first cut is along the medial cortex; subsequently, with the leg held in abduction, the lateral portion of the cortex is cut. Osteotomy of the posterior column is performed at an angle of 120 degrees to the previous iliac cut. Fluoroscopy may be used to confirm safe depth and trajectory. As with the iliac osteotomy, the posterior column cut begin within the medial cortex. The cut may be initiated using a straight or angled osteotome depending on the body habitus and angle of the osteotomy plane. To ensure that the retro-acetabular portion is complete, a straight osteotome is passed in a distal-ward direction; likewise, a Ganz-type osteotome

is passed from the inside of the pelvis aiming laterally in sequential steps. Tactile and aural feedback is important at this step, and the bone may displace subtly during progressive osteotomy maneuvers. Maintaining a safe distance from the subchondral bone prevents iatrogenic intra-articular fracture propagation.

A laminar spreader is placed into the iliac osteotomy site; a second laminar spreader may be placed in the second limb of the retro-acetabular osteotomy to effect the final displacement. Residual tethering of the posterior column osteotomy, if present, may be freed under direct vision with an angled bifid osteotome from the inside. During this maneuver the hip is again extended and abducted to relax the sciatic nerve.

Acetabular correction

A Schanz screw (5.0 mm) is inserted into the superior aspect of the mobile fragment, and rotatory motions test the osteotomy segment mobility. Combined movement of the Schanz screw and an inwards turn of the laminar spreader placed at the vertex of the supra-retro-acetabular osteotomy may help to free the fragment and maintain an adequate reorientation. A small bone hook or Weber clamp may be applied to the pubic segment to aid in reduction. The lack of complete mobility prompts the surgeon to review three problematic sites: The pubic osteotomy and accompanying periosteum, the posterior cortex at the vertex (junction of iliac and posterior column segments), and the inferior ischial cut. Mobility is again verified with the ability to flip the fragment.

The reorientation is then performed, keeping in mind that there is one ideal position of the fragment that optimizes joint loading conditions, while maintaining range of motion about an ideal center of hip rotation. For the more common hip dysplasia morphology, the acetabulum is usually repositioned with a combination of internal rotation, forward tilt/extension, and medial translation. As before, adjunctive reorientation tools may include a ball-spike pusher, Weber clamp, small bone hook, or a second Schanz pin. Provisional fixation is maintained with several terminally threaded or smooth Kirschner wires; the surgeon may choose to place two antegrade and one retrograde wires.

A properly projected and rotated pelvic radiograph is then obtained intra-operatively. This X-ray must be critically evaluated for the final acetabular orientation: The lateral center-edge angle, Tönnis angle/inclination, adequate medialization of the hip center of rotation, teardrop position, restoration of Shenton's line, and version of the acetabulum. It is essential to not retrovert the acetabulum in addressing classic dysplasia. An example of an acetabular correction performed for hip dysplasia is presented in Figure 2.

On-table range of motion is then performed to assess for potential secondary impingement or residual instability after the acetabular correction. The hip flexion should be at least 100 degrees. The mobile segment is secured with several 3.5 mm/4.5 mm fully

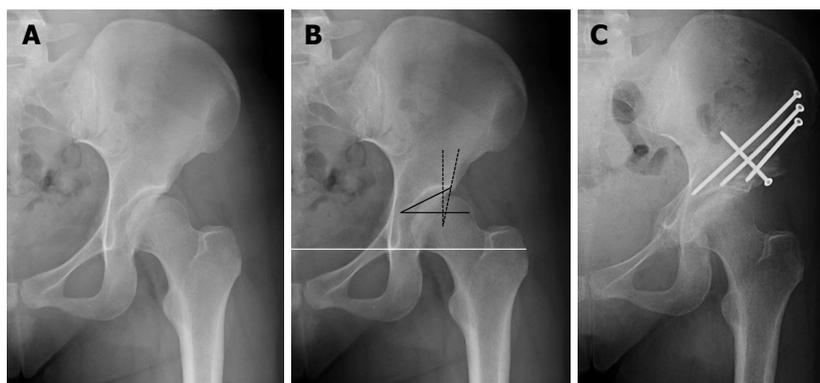


Figure 2 Acetabular radiographic measurements and correction. Pre-operative (A) antero-posterior radiograph of a hip with classic dysplastic. Basic radiographic measurements of dysplasia (B) include the lateral center edge angle (dashed black line; measure of lateral acetabular coverage), Tönnis angle (solid black line; measure of sourcil angle); the solid white line is the inter-teardrop line, which is the reference for pelvic tilt in the coronal plane; an anterior center edge angle on a false profile view completes the basic radiographic work-up. The post-operative (C) antero-posterior radiographic view of the same hip demonstrating satisfactory acetabular reorientation to correct bony dysplasia.

threaded screws in antegrade and/or retrograde fashion. Fluoroscopic images may confirm that the acetabular reduction is maintained, along with position of fixation hardware.

After fragment fixation, an arthrotomy may be performed. This offers the opportunity to examine the acetabular labrum for repair if needed, as well as to address any offset abnormalities of the femoral neck region. Labral debridement vs repair (with possible augmentation) is performed, depending on the characteristics of the labral tear and quality of tissue. Osteochondroplasty using a curved osteotome and a burr may be performed at this time at the sites of femoro-acetabular impingement.

Wound closure

After thorough irrigation of the joint and surgical field, the capsular incision is closed. Any bony prominences of the reoriented fragment may be trimmed with a saw and/or burr; the autograft may be used to fill the iliac osteotomy site. The rectus tendon is repaired with non-absorbable suture back to its footprint. The subspine region may be decompressed if impinging on the femur in deep flexion. The ASIS fragment is repositioned and fixed with a small-fragment screw or heavy suture in trans-osseous fashion. Closed suction drains may be used per surgeon preference. The fascia over the iliac wing, as well as distally over the tensor, is closed. Establishing a watertight seal of the fascia is important. The remainder of the superficial wound is closed in a routine, layered fashion.

POST-OPERATIVE CARE AND REHABILITATION

Mobility and weight-bearing status depends on whether the PAO has been performed alone or in conjunction with other procedures, such as femoral osteotomy and/or surgical hip dislocation. With maintenance of the

posterior column and with good bone quality, partial weight-bearing (15 kg) is prescribed for the first 4-6 wk. A period of non-weight-bearing may be used in the setting of large corrections or poor bone quality. A continuous passive motion machine may be employed, especially if intra-articular work is performed. Routine deep venous thrombosis prophylaxis (*e.g.*, low molecular weight heparin or aspirin) is used for the first six weeks. Heterotopic ossification prophylaxis is not routinely used. At four weeks, abduction strengthening exercises (first standing and then laying on opposite hip) is allowed, along with a stationary bike. Active flexion of the hip joint is prohibited for at least six weeks to protect the reattached hip flexor muscles. At eight weeks postoperatively, the patient is assessed clinically and radiographically: Healing is usually sufficient for full weight-bearing, and full muscular strengthening can be started. Flexion strength may take up to six months to return, and complete bony union will take several months to achieve. The majority of patients have pain-free range of motion at 2-3 mo, depending on how significant of a correction has been performed. Patients may generally return to sports activity between 6-12 mo, but patients with severe preexisting abductor and other functional weakness may take up to a year for complete rehabilitation.

CONCLUSION

The Bernese PAO is one of several acetabular osteotomies to address structural deformity in patients with closed triradiate cartilage, including adolescents and young adults with symptomatic dysplasia. The PAO technique involves a modified Smith-Petersen approach. Advantages of the Bernese PAO include preservation of the weight-bearing posterior column of the acetabulum, preservation of the acetabular blood supply, maintenance of the hip abductor musculature, and powerful deformity correction about an ideal center of rotation.

The Bernese PAO has been applied to complex acetabular dysplasia cases for over 30 years^[5]. While it remains a technically demanding procedure^[6-8], the potential to improve the natural history of hip dysplasia is well-demonstrated in mid- and long-term clinical studies^[9-11]. Refinements in surgical technique and patient indications, in combination with the application of key femoroacetabular impingement concepts, have increased the understanding of hip pathomorphology and the parameters for acetabular reorientation^[12].

Compared with a number of other pelvic osteotomy techniques, the Bernese PAO maintains the posterior column. By not violating the posterior column, prolonged immobilization and/or extensive pelvic fixation methods are obviated, and there remains inherent stability and good potential for union of the mobile fragment to the residual pelvis. The juxta-articular osteotomy planes also maintain the dimensions of the true pelvis and effects a powerful correction about an ideal center of hip rotation. With medialization of the hip joint, the abductor lever arm is maximized, and joint reaction forces are dampened.

Since its initial description, the PAO surgical technique has undergone various modifications^[13]. The original approach involved stripping of the abductors from the iliac crest during the iliac and supra-acetabular osteotomy segment. Protecting the abductors not only preserves muscle function but also decreases the risk of osteonecrosis due to compromised acetabular vascular supply. Associated vessels include branches of the obturator, superior and inferior gluteal arteries, and capsular contributions to acetabular perfusion. Initially, the bone cuts were performed from both sides of the iliac wing; the bone cuts are now predominantly performed from the inner aspect of the pelvis to further preserve the abductors. More recently, it has become apparent that hip flexion strength is decreased post-operatively, and thus a rectus-sparing approach has been supported by some centers. This technique variation leaves the direct and indirect heads of the rectus femoris attached. It is unclear whether this will solve the problem of flexion strength deficits, or whether injury to the most proximal branches of the femoral nerve during osteotomy of the pubis may be increased.

Other modifications to the original surgical technique include a two-incision technique. In this manner, the ischial osteotomy has been performed under direct visualization. The primary disadvantage of this technique involves dissection of the external rotators posteriorly, with risk to the medial femoral circumflex artery and blood supply to the femoral head. Additional variations to the technique include various minimally invasive incisions, including a trans-sartorial approach. Other investigators have presented the use of hip arthroscopy at the time of PAO to evaluate the articular cartilage and to address labral pathology, which obviates the need for capsulotomy and more distal exposure.

The femoral head in a dysplastic hip may have a decreased head-neck offset and lateral flattening from a

hypertrophic gluteus minimus. When the acetabulum is reoriented in a position of excess lateral and/or anterior coverage, secondary femoroacetabular impingement may occur. Impingement has been recognized as a potential cause for continued pain after PAO. As a result, an arthrotomy (or hip arthroscopy as above) has been incorporated for evaluation and correction of intra-articular impingement. Careful recognition of acetabular version (*e.g.*, avoidance of iatrogenic retroversion) during the correction also helps to minimize secondary impingement.

The osteotomy technique is technically demanding, yet offers reproducible results with good long-term survivorship in carefully selected patients with preserved cartilage and the ability to meet rehabilitation demands. Pelvic osteotomy should be considered as a preferred alternative to arthroplasty in the young, active patient with correctable structural deformity of the hip.

REFERENCES

- 1 **Leunig M**, Siebenrock KA, Ganz R. Rationale of periacetabular osteotomy and background work. *Instr Course Lect* 2001; **50**: 229-238 [PMID: 11372318]
- 2 **Clohisey JC**, Carlisle JC, Beaulé PE, Kim YJ, Trousdale RT, Sierra RJ, Leunig M, Schoenecker PL, Millis MB. A systematic approach to the plain radiographic evaluation of the young adult hip. *J Bone Joint Surg Am* 2008; **90** Suppl 4: 47-66 [PMID: 18984718 DOI: 10.2106/JBJS.H.00756]
- 3 **Ganz R**, Klaue K, Vinh TS, Mast JW. A new periacetabular osteotomy for the treatment of hip dysplasias. Technique and preliminary results. *Clin Orthop Relat Res* 1988; (**232**): 26-36 [PMID: 3383491]
- 4 **Pring ME**, Trousdale RT, Cabanela ME, Harper CM. Intraoperative electromyographic monitoring during periacetabular osteotomy. *Clin Orthop Relat Res* 2002; (**400**): 158-164 [PMID: 12072758 DOI: 10.1097/00003086-200207000-00020]
- 5 **Clohisey JC**, Schutz AL, St John L, Schoenecker PL, Wright RW. Periacetabular osteotomy: a systematic literature review. *Clin Orthop Relat Res* 2009; **467**: 2041-2052 [PMID: 19381741 DOI: 10.1007/s11999-009-0842-6]
- 6 **Thawrani D**, Sucato DJ, Podeszwa DA, DeLaRocha A. Complications associated with the Bernese periacetabular osteotomy for hip dysplasia in adolescents. *J Bone Joint Surg Am* 2010; **92**: 1707-1714 [PMID: 20660233 DOI: 10.2106/JBJS.I.00829]
- 7 **Peters CL**, Erickson JA, Hines JL. Early results of the Bernese periacetabular osteotomy: the learning curve at an academic medical center. *J Bone Joint Surg Am* 2006; **88**: 1920-1926 [PMID: 16951106 DOI: 10.2106/JBJS.E.00515]
- 8 **Hussell JG**, Rodriguez JA, Ganz R. Technical complications of the Bernese periacetabular osteotomy. *Clin Orthop Relat Res* 1999; (**363**): 81-92 [PMID: 10379308 DOI: 10.1097/00003086-19990600-00011]
- 9 **Steppacher SD**, Tannast M, Ganz R, Siebenrock KA. Mean 20-year followup of Bernese periacetabular osteotomy. *Clin Orthop Relat Res* 2008; **466**: 1633-1644 [PMID: 18449617 DOI: 10.1007/s11999-008-0242-3]
- 10 **Troelsen A**, Elmengaard B, Søballe K. Medium-term outcome of periacetabular osteotomy and predictors of conversion to total hip replacement. *J Bone Joint Surg Am* 2009; **91**: 2169-2179 [PMID: 19723994 DOI: 10.2106/JBJS.H.00994]
- 11 **Matheny T**, Kim YJ, Zurakowski D, Matero C, Millis M. Intermediate to long-term results following the Bernese periacetabular osteotomy and predictors of clinical outcome. *J Bone Joint Surg Am* 2009; **91**: 2113-2123 [PMID: 19723987 DOI: 10.2106/JBJS.G.00143]

- 12 **Siebenrock KA**, Leunig M, Ganz R. Periacetabular osteotomy: the Bernese experience. *Instr Course Lect* 2001; **50**: 239-245 [PMID: 11372320]
- 13 **Leunig M**, Ganz R. Evolution of technique and indications for the Bernese periacetabular osteotomy. *Bull NYU Hosp Jt Dis* 2011; **69** Suppl 1: S42-S46 [PMID: 22035484]

P- Reviewer: Konya MN, Papachristou GC, Robertson GA
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Liu SQ



Controversial role of arthroscopic meniscectomy of the knee: A review

Austin Y Ha, Robert M Shalvoy, Anne Voisinet, Jennifer Racine, Roy K Aaron

Austin Y Ha, Robert M Shalvoy, Anne Voisinet, Jennifer Racine, Roy K Aaron, Department of Orthopaedic Surgery, Warren Alpert Medical School of Brown University, Providence, RI 02906, United States

Author contributions: Ha AY contributed to the study conception and design, the acquisition, analysis, and interpretation of data, and the drafting of the manuscript; Shalvoy RM contributed to the analysis and interpretation of data and critically revised the manuscript; Voisinet A and Racine J contributed to the acquisition and analysis of data; Aaron RK contributed to the study conception and design, the acquisition, analysis, and interpretation of data, the drafting of the manuscript, as well as the critical revision of the manuscript.

Conflict-of-interest statement: The authors have no conflict of interest to disclose.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Roy K Aaron, MD, Professor, Department of Orthopaedic Surgery, Warren Alpert Medical School of Brown University, 100 Butler Drive, Providence, RI 02906, United States. roy_aaron@brown.edu
Telephone: +1-401-8615832

Received: June 29, 2015

Peer-review started: July 2, 2015

First decision: August 25, 2015

Revised: January 13, 2016

Accepted: January 27, 2016

Article in press: January 29, 2016

Published online: May 18, 2016

Abstract

The role of arthroscopic partial meniscectomy (APM) in reducing pain and improving function in patients with meniscal tears remains controversial. Five recent high-quality randomized controlled trials (RCTs) compared non-operative management of meniscal tears to APM, with four showing no difference and one demonstrating superiority of APM. In this review, we examined the strengths and weaknesses of each of these RCTs, with particular attention to the occurrence of inadvertent biases. We also completed a quantitative analysis that compares treatment successes in each treatment arm, considering crossovers as treatment failures. Our analysis revealed that each study was an excellent attempt to compare APM with non-surgical treatment but suffered from selection, performance, detection, and/or transfer biases that reduce confidence in its conclusions. While the RCT remains the methodological gold standard for establishing treatment efficacy, the use of an RCT design does not in itself ensure internal or external validity. Furthermore, under our alternative analysis of treatment successes, two studies had significantly more treatment successes in the APM arm than the non-operative arm although original intention-to-treat analyses showed no difference between these two groups. Crossovers remain an important problem in surgical trials with no perfect analytical solution. With the studies available at present, no conclusion can be drawn concerning the optimal treatment modality for meniscal tears. Further work that minimizes significant biases and crossovers and incorporates sub-group and cost-benefit analyses may clarify therapeutic indications.

Key words: Arthroscopic partial meniscectomy; Meniscal tear; Knee osteoarthritis; Physical therapy; Randomized controlled trial; Crossover; Bias

© The Author(s) 2016. Published by Baishideng Publishing

Group Inc. All rights reserved.

Core tip: Despite several recent high-quality randomized controlled trials, the efficacy of arthroscopic partial meniscectomy (APM) for meniscal tears remains controversial. In this review, we analyzed the five most important trials for potential inadvertent biases. Each study was found to have some combination of selection, performance, detection, and transfer biases that compromise its conclusion. We also completed an alternative analysis of their results that took into account the observed high crossover rates. This analysis suggested that two studies whose original conclusions showed no superiority of APM may in fact support APM.

Ha AY, Shalvoy RM, Voisinnet A, Racine J, Aaron RK. Controversial role of arthroscopic meniscectomy of the knee: A review. *World J Orthop* 2016; 7(5): 287-292 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/287.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.287>

INTRODUCTION

Observational studies, including longitudinal cohort studies, have suggested that arthroscopic partial meniscectomy (APM) is an effective treatment for meniscal tears^[1-5]. More recent randomized controlled trials (RCTs) have suggested that non-operative regimens may provide equivalent symptom relief and functional improvement^[6-10]. We have previously analyzed RCTs comparing APM with non-operative therapy specifically in the clinical setting of meniscal tears with concomitant osteoarthritis of the knee (MT-OAK) (Ha *et al*, submitted). That approach maximized internal validity but limited generalizability of the analysis. Therefore, there is value in analyzing reports of APM in a variety of clinical settings, understanding that the variable settings may increase variability but are more broadly generalizable. Occasionally, direct comparisons between outcome assessments cannot be made because of varying assessment instruments but outcomes can still be compared.

Our previous analysis of APM for MT-OAK identified two types of problems in the studies reviewed that compromised confidence in the study conclusions: (1) inadvertent biases within the structure of the RCTs; and (2) the large numbers of patients who crossed over from the non-operative to the operative groups. While the RCT is the methodological gold standard for establishing efficacy of treatments, bias may still occur within their structure that compromise their conclusions^[11-15]. The second problem encountered is the evaluation of outcomes of patients who cross over from one treatment group to another, when they comprise a substantial portion of the study population^[16]. Crossovers can be major confounders especially to an intention to treat (ITT) analysis and can obscure differences in the outcomes

of two treatments^[16,17]. Other methods of data analysis, each with their own limitations, may be useful as supplementary, but potentially more precise, analytical approaches^[14].

In the present analysis, we review five RCTs reporting the efficacy of APM for meniscal tears in a variety of clinical settings. Particular attention is paid to the occurrence of biases within the RCT structure and the fidelity to the treatment assignment. Second, we employ an alternative quantitative analysis that examines the effects of crossovers upon the efficacy of APM.

Five RCTs comparing APM to non-operative treatment for meniscal tears with at least 6 mo follow-up were included in this analysis^[6-10,18]. One study was excluded because it had not reported results beyond 3 mo^[19]. Another study was excluded because it dealt with arthroscopic surgery for OAK rather than meniscal tears^[20]. A third study was excluded whose results are not generally accepted because of methodological flaws making the data uninterpretable^[21].

The five RCTs were first assessed for the presence of inadvertent bias within their structure. We used the framework proposed by Rudicel *et al*^[15] to detect existing selection, performance, detection, or transfer biases. Furthermore, each RCT was individually assessed for the percentage of patients meeting the criterion for treatment success in both non-operative and APM groups. For this analysis, we used the definition of treatment success put forward by Katz *et al*^[8]: Achieving improvement that is equal to or greater than the minimal clinically important difference (MCID) at the primary outcome time point compared to baseline without crossing over or requiring additional procedures. Data from either the original report or supplementary information provided directly by the authors was used to complete this analysis.

The Fisher exact test was used to test for statistical significance between the numbers of treatment successes in operative and nonoperative groups. SPSS, version 23.0 (IBM), was used for all statistical analyses. A biomedical statistician performed the statistical analyses.

The citations, meniscal pathology and associated conditions of the five RCTs reviewed are summarized in Table 1.

Herrlin *et al*^[6,7] reported 96 patients with medial meniscal tears and Ahlback grade 0-1 osteoarthritis (comparable to Kellgren-Lawrence grade 0-2) between the ages of 45-64 followed for 5 years. The primary outcome was the change in knee injury and osteoarthritis outcome (KOOS) scores at 6-mo follow-up. Forty-seven were randomized to APM and exercise; 49 were randomized to exercise therapy alone. Thirteen/forty-nine (27%) of patients managed by exercise therapy were ultimately treated by APM. ITT analysis showed a 9-point difference on the KOOS Pain scale compared to baseline favoring APM, which was not statistically significant. Forty-two/forty-seven (89%) of operative group met the definition for treatment

Table 1 Characteristics of included studies

Ref.	Meniscal pathology	Associated osteoarthritis	Operative group treatment	Non-operative group treatment
Herrlin <i>et al</i> ^[6,7]	Medial meniscal tear	Ahlback grades 0-1	Exercise + APM	Exercise
Katz <i>et al</i> ^[8]	Meniscal tear	Kellgren-Lawrence grades 0-3	Exercise + APM	Exercise
Yim <i>et al</i> ^[10]	Horizontal medial meniscal tear	Kellgren-Lawrence grades 0-1	APM	Strength exercises
Sihvonen <i>et al</i> ^[9]	Meniscal tear	Kellgren-Lawrence grades 0-1	APM	Sham surgery
Gauffin <i>et al</i> ^[18]	Meniscal tear	Kellgren-Lawrence grades 0-2	Exercise + APM	Exercise

APM: Arthroscopic partial meniscectomy.

success compared to 34/49 (69%) of non-operative group ($P = 0.023$) (personal communication, May 18, 2015). The study had significant strengths including a homogeneous population and well standardized surgical and physical therapy protocols. However, the APM cohort had significantly poorer baseline characteristics, leading to possible selection bias. The study also experienced low enrollment of eligible patients (80/177, or 55%), high crossover rate, and was non-blinded.

Katz *et al*^[8,16] followed for 12 mo 351 patients with meniscal tears and concomitant osteoarthritis of grades 0-3 by Kellgren-Lawrence criteria aged 45 years or older. The primary outcome was the change in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores at 6-mo follow-up. One hundred and seventy-four were assigned to APM and physical therapy; 177 were assigned to physical therapy alone. 51/177 (29%) and 59/177 (33%) of patients initially managed by physical therapy underwent APM by 6 mo and 12 mo, respectively. ITT analysis showed a 2.4-point difference in on the WOMAC score compared to baseline favoring APM, which was not statistically significant. However, as noted in the original paper, a greater proportion of APM patients had successful treatment outcomes than that of physical therapy patients (108/161, or 67.1% vs 74/169, or 43.8%, $P < 0.0001$). This was a landmark study with a strong study design and large cohort size. However, this study suffers from low enrollment rate (351/1330, or 26%), inconsistent referral patterns from participating surgeons, and lack of blinding, leading to potential selection and detection biases. High crossover rate and large variability in the percentage of crossovers among participating centers (range 0%-60%) question protocol adherence and suggest potential performance and transfer biases.

Yim *et al*^[10] reported 102 patients aged 43-62 years with degenerative horizontal tears of the posterior horn of the medial meniscus with OA of grades 0-1 by Kellgren-Lawrence criteria followed for 24 mo. The primary outcome was by Lysholm scores at 2 years follow-up. Fifty patients were treated with APM and strengthening exercises; 52 were treated with strengthening exercises alone. Only 1/52 (2%) of patients assigned to nonoperative management crossed over to surgery. The results as analyzed in the original report showed no difference in the Lysholm scores between the two groups at 2 years follow-up. Forty-five/fifty (90%) of surgical patients met the definition for treatment success

compared to 48/52 (92%) of non-surgical patients ($P = 0.739$) (personal communication, June 27, 2015). The strengths of this study include low loss to follow-up rate (2/108, or 2%), low crossover rate (1/52, or 2%), and relatively long follow-up period. Its weaknesses include: disproportionately large female study population (81/102, or 79.4%); sample size falling just short of the 54 patients per group required for 80% power; and low enrollment rate (108/162, or 66.7%). Finally, Lysholm scores are best suited for measuring outcomes after ligament surgery and may not have sufficient validity, sensitivity, and reliability for assessing degenerative tears of the meniscus^[22].

Sihvonen *et al*^[9] reported 146 patients aged 35-65 years with degenerative meniscal tears with OA of grades 0-1 by Kellgren-Lawrence criteria followed for 12 mo. The primary outcome measures were changes in the Lysholm and Western Ontario Meniscal Evaluation Tool (WOMET) scores at 12 mo post-op. Seventy patients were treated with APM; 76 underwent sham surgery. Five/seventy-six (6.6%) of patients assigned to sham surgery were ultimately treated with APM (4 patients) or high tibial osteotomy (1 patient). Two/seventy (2.9%) of patients assigned to APM were ultimately treated with additional arthroscopy (1 patient) or total knee replacement (1 patient). The results as analyzed in the report showed no differences in the changes in WOMET and Lysholm scores at 12 mo compared to baseline. A priori and post-hoc subgroup analyses did not show between-group differences. Forty-nine/seventy (70%) of the APM cohort met the definition for treatment success compared to 51/76 (67.1%) of the exercise cohort ($P = 0.725$) (personal communication, May 11, 2015). This study had many strengths, including its rigorous double-blinded, sham-controlled design, low loss to follow-up and crossover rates, and high enrollment rate (146/205, or 71.2%). This study's weakness is its relatively narrow generalizability, having included only nontraumatic degenerative medial meniscal tears with no or very mild OA.

Gauffin *et al*^[18] reported 150 patients aged 45-64 years with minimum 3 mo of meniscal symptoms and OA of grades 0-2 by Kellgren-Lawrence criteria, who had undergone 3 mo of prior physiotherapy, followed for 12 mo. The primary outcome measure was the change in KOOS Pain scores at 12 mo compared to baseline. Seventy-five patients were treated with arthroscopic surgery, and 75 patients were treated

by 3 mo of physical exercises alone. Sixteen/seventy-five (21.3%) of patients assigned to physical therapy ultimately underwent surgery, whereas 9/75 (12%) originally assigned to surgery only completed physical exercises. This is the first RCT to report superiority of surgical management to physical therapy, by both ITT and as-treated analyses. In ITT analysis, the between-group difference in the changes in KOOS Pain scores from baseline was both statistically and clinically significant (10.6 points, $P = 0.004$). As-treated analysis accentuated this difference to 13.9 points ($P < 0.001$). However, the surgery group had more females and poorer baseline KOOS scores than the non-surgery group - a breakdown of randomization. Sixty-two/seventy-four (84%) of the surgical patients, whereas 36/56 (64%) of the non-surgical patients, met the definition for treatment success ($P = 0.010$). This study's strengths include a high enrollment rate (150/179, or 83.8%), relatively long planned follow-up period of 3 years. The study's weaknesses include heterogeneity in the surgeries performed, poor compliance to physiotherapy, and high loss to follow-up rate (20/150, or 13.3%) and crossover.

DISCUSSION

While RCTs are the best way to minimize bias in clinical trials, there are nonetheless opportunities for bias within the structure of an RCT and the use of this study design in itself does not ensure either internally or externally valid data^[12]. Analysis of five RCTs reveals that they were excellent attempts to compare APM with non-surgical treatment but all suffered from potential inadvertent biases that reduce confidence in their conclusions.

Selection bias was the most frequently encountered bias in the five RCTs. This was often due to a low enrollment rate from the patients' explicit preference for one treatment option to the other. Two studies suffered from unequal baseline characteristics between the surgical and non-surgical arms despite randomization. Performance bias was observed when intraoperative procedures and/or physiotherapy protocols were not standardized or determined a priori. Variability in supplemental therapy, such as unspecified use of non-steroidal anti-inflammatory drugs, and inconsistency among different participating medical centers can also lead to performance bias. Detection bias was also common, as only one RCT employed the double-blind methodology. We acknowledge that double blinding in surgical trials is challenging. However, a placebo effect may account for a significant part of response to surgery - up to 35% in some trials^[23,24] - and therefore needs to be addressed^[25]. Placebo also contributes to the effect of physical therapy and may need to be controlled^[26,27]. Lastly, transfer bias occurs when there is a significant proportion of patients lost to follow-up or crossing over to the opposite study arm. One RCT had a high loss to follow-up rate, and three RCTs suffered from high

crossover rates.

The American Academy of Orthopedic Surgeons has recommended using the MCID to evaluate the clinical significance of treatment outcomes^[28]. The MCID is the smallest change in an outcome score that corresponds to a change in a patient's condition and thereby derives its clinical relevance. The MCIDs of two of the patient report outcome measures used in these studies, the WOMAC and the KOOS, have been determined to be 9-12 points and 8-10 points respectively^[22]. We analyzed each study according to the number of patients in each group reaching this clinically meaningful end point.

Using the definition of treatment success suggested by Katz *et al*^[8], which occurs when the improvement in a patient's outcome score is greater than or equal to the MCID without crossing over or requiring additional procedures, and the data reported in the original papers or communicated to us directly by the authors, we compared the percentage of patients meeting the definition of treatment success in each group for statistical significance. Two RCTs had significantly more patients treated successfully with APM, although their original ITT analyses showed no between-group differences. By this analysis method, three RCTs favor APM and two RCTs show no difference (Table 2).

ITT analysis remains the current gold standard for data analysis in RCTs. It has the advantages of preserving randomization and minimizing false positive (type I) errors; however, in the setting of high cross over rates, the ITT analysis does not reflect the treatment actually received and, therefore, may not accurately reflect the efficacy of treatment, leading to false negative (type II) errors^[29,30]. The risk for a type II error is especially high when there is a significant number of patients who perform poorly with one treatment method and then show rapid improvement after crossing over. Noncompliance with assigned therapy may also exaggerate this feature and lead the ITT analysis to underestimate the potential benefit of a treatment. Additional analyses may therefore be useful^[31,32]. An "as treated" analysis is an alternative, but it has been criticized for compromising initial randomization. Our analysis of treatment success can be considered a form of "as treated" analysis as it separates those patients who remained in their originally assigned groups from those who did not. However, we acknowledge that this analysis is not a generic solution to the crossover problem.

CONCLUSION

This review sought to approach the question of efficacy of APM and non-operative management for meniscal tears by examining five important RCTs. Special attention was paid to inadvertent biases they may harbor despite their RCT design. Many potential biases were identified. An alternative analysis to the conventional ITT analysis was completed, which showed that the data from three RCTs favor APM while two others show

Table 2 Outcomes of analysis

Ref.	Potential bias	Results as reported	Crossovers <i>n</i> (%)	Treatment success by group
Herrlin <i>et al</i> ^[6,7]	Selection Detection Transfer	APM group showed 9-point greater improvement in KOOS pain scores (NS)	13/49 (27%) from PT to APM	APM - 42/47 (89%) PT - 34/49 (69%) (<i>P</i> = 0.023)
Katz <i>et al</i> ^[8]	Selection Performance Detection Transfer	APM group showed 2.4-point greater improvement in WOMAC scores (NS)	51/177 (29%) from PT to APM at 6 mo post-op	APM - 108/161 (67%) PT - 74/169 (44%) (<i>P</i> < 0.0001)
Yim <i>et al</i> ^[10]	Selection Detection	APM group showed 0.1-point greater improvement in Lysholm scores (NS)	1/52 (2%) from PT to APM	APM - 45/50 (90%) PT - 48/52 (92%) (<i>P</i> = 0.739)
Sihvonen <i>et al</i> ^[9]	Narrow generalizability	Sham surgery group showed 2.5-point greater improvement in WOMET scores (NS)	5/76 (6.6%) from sham to APM	APM - 49/70 (70%) Sham - 51/76 (67%) (<i>P</i> = 0.725)
Gauffin <i>et al</i> ^[18]	Performance Detection Transfer	APM group showed 10.6-point greater improvement on KOOS Pain scores (<i>P</i> = 0.004)	16/75 (21%) from PT to APM 9/75 (12%) from APM to PT	APM - 62/74 (84%) PT - 36/56 (64%) (<i>P</i> = 0.010)

APM: Arthroscopic partial meniscectomy; NS: Not statistically significant; KOOS: Knee injury and osteoarthritis outcome; WOMAC: Western Ontario and McMaster Osteoarthritis Index; WOMET: Western Ontario Meniscal Evaluation Tool; PT: Physical therapy.

no difference between APM and non-operative management. Use of the RCT design in itself ensures neither internal nor external validity of study data. Crossovers remain a significant problem in surgical RCTs, but there are currently no suitable analytical methods that both preserve randomization and minimize type II errors. With the studies available at present, no conclusion can be drawn concerning the optimal treatment modality for meniscal tears. Further work on sub-group analysis and cost-benefit analysis may clarify therapeutic indications.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Herrlin, Dr. Kim, Dr. Seon, Dr. Yim, Dr. Sihvonen, and Dr. Järvinen for providing supplemental data about their published trials. We would also like to thank Dr. Kristina Monteiro for her help with the statistical analyses.

REFERENCES

- Aaron RK, Skolnick AH, Reinert SE, Ciombor DM. Arthroscopic débridement for osteoarthritis of the knee. *J Bone Joint Surg Am* 2006; **88**: 936-943 [PMID: 16651566 DOI: 10.2106/jbjs.d.02671]
- Burks RT, Metcalf MH, Metcalf RW. Fifteen-year follow-up of arthroscopic partial meniscectomy. *Arthroscopy* 1997; **13**: 673-679 [PMID: 9442319 DOI: 10.1016/S0749-8063(97)90000-1]
- Chatain F, Robinson AH, Adeleine P, Chambat P, Neyret P. The natural history of the knee following arthroscopic medial meniscectomy. *Knee Surg Sports Traumatol Arthrosc* 2001; **9**: 15-18 [PMID: 11269578 DOI: 10.1007/s001670000146]
- Matsusue Y, Thomson NL. Arthroscopic partial medial meniscectomy in patients over 40 years old: a 5- to 11-year follow-up study. *Arthroscopy* 1996; **12**: 39-44 [PMID: 8838727 DOI: 10.1016/s0749-8063(96)90217-0]
- Roos EM, Roos HP, Ryd L, Lohmander LS. Substantial disability 3 months after arthroscopic partial meniscectomy: A prospective study of patient-relevant outcomes. *Arthroscopy* 2000; **16**: 619-626 [PMID: 10976123 DOI: 10.1053/jars.2000.4818]
- Herrlin S, Hållander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 393-401 [PMID: 17216272 DOI: 10.1007/s00167-006-0243-2]
- Herrlin SV, Wange PO, Lapidus G, Hållander M, Werner S, Weidenhielm L. Is arthroscopic surgery beneficial in treating non-traumatic, degenerative medial meniscal tears? A five year follow-up. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 358-364 [PMID: 22437659 DOI: 10.1007/s00167-012-1960-3]
- Katz JN, Brophy RH, Chaisson CE, de Chaves L, Cole BJ, Dahm DL, Donnell-Fink LA, Guermazi A, Haas AK, Jones MH, Levy BA, Mandl LA, Martin SD, Marx RG, Miniaci A, Matava MJ, Palmisano J, Reinke EK, Richardson BE, Rome BN, Safran-Norton CE, Skoniecki DJ, Solomon DH, Smith MV, Spindler KP, Stuart MJ, Wright J, Wright RW, Losina E. Surgery versus physical therapy for a meniscal tear and osteoarthritis. *N Engl J Med* 2013; **368**: 1675-1684 [PMID: 23506518 DOI: 10.1056/NEJMoa1301408]
- Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Nurmi H, Kalske J, Järvinen TL. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. *N Engl J Med* 2013; **369**: 2515-2524 [PMID: 24369076 DOI: 10.1056/NEJMoa1305189]
- Yim JH, Seon JK, Song EK, Choi JI, Kim MC, Lee KB, Seo HY. A comparative study of meniscectomy and nonoperative treatment for degenerative horizontal tears of the medial meniscus. *Am J Sports Med* 2013; **41**: 1565-1570 [PMID: 23703915 DOI: 10.1177/0363546513488518]
- Chan S, Bhandari M. The quality of reporting of orthopaedic randomized trials with use of a checklist for nonpharmacological therapies. *J Bone Joint Surg Am* 2007; **89**: 1970-1978 [PMID: 17768194 DOI: 10.2106/JBJS.F.01591]
- Cowan J, Lozano-Calderón S, Ring D. Quality of prospective controlled randomized trials. Analysis of trials of treatment for lateral epicondylitis as an example. *J Bone Joint Surg Am* 2007; **89**: 1693-1699 [PMID: 17671006 DOI: 10.2106/JBJS.F.00858]
- Laupacis A, Rorabeck CH, Bourne RB, Feeny D, Tugwell P, Sim DA. Randomized trials in orthopaedics: why, how, and when? *J Bone Joint Surg Am* 1989; **71**: 535-543 [PMID: 2703513]
- Losina E, Wright J, Katz JN. Clinical trials in orthopaedics research. Part III. Overcoming operational challenges in the design and conduct of randomized clinical trials in orthopaedic surgery. *J Bone Joint Surg Am* 2012; **94**: e35 [PMID: 22438008 DOI: 10.2106/JBJS.K.00009]
- Rudicel S, Esdaile J. The randomized clinical trial in orthopaedics: obligation or option? *J Bone Joint Surg Am* 1985; **67-A**: 1284-1293 [PMID: 11650735]

- 16 **Katz JN**, Losina E, Lohmander LS. OARSI Clinical Trials Recommendations: Design and conduct of clinical trials of surgical interventions for osteoarthritis. *Osteoarthritis Cartilage* 2015; **23**: 798-802 [PMID: 25952350 DOI: 10.1016/j.joca.2015.02.024]
- 17 **Xie H**, Heitjan DF. Sensitivity analysis of causal inference in a clinical trial subject to crossover. *Clin Trials* 2004; **1**: 21-30 [PMID: 16281459 DOI: 10.1191/1740774504cn005oa]
- 18 **Gauffin H**, Tagesson S, Meunier A, Magnusson H, Kvist J. Knee arthroscopic surgery is beneficial to middle-aged patients with meniscal symptoms: a prospective, randomised, single-blinded study. *Osteoarthritis Cartilage* 2014; **22**: 1808-1816 [PMID: 25086401 DOI: 10.1016/j.joca.2014.07.017]
- 19 **Stensrud S**, Risberg MA, Roos EM. Effect of exercise therapy compared with arthroscopic surgery on knee muscle strength and functional performance in middle-aged patients with degenerative meniscus tears: a 3-mo follow-up of a randomized controlled trial. *Am J Phys Med Rehabil* 2015; **94**: 460-473 [PMID: 25299520 DOI: 10.1097/PHM.0000000000000209]
- 20 **Kirkley A**, Birmingham TB, Litchfield RB, Giffin JR, Willits KR, Wong CJ, Feagan BG, Donner A, Griffin SH, D'Asciano LM, Pope JE, Fowler PJ. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008; **359**: 1097-1107 [PMID: 18784099 DOI: 10.1056/NEJMoa0708333]
- 21 **Moseley JB**, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, Hollingsworth JC, Ashton CM, Wray NP. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002; **347**: 81-88 [PMID: 12110735 DOI: 10.1056/nejmoa013259]
- 22 **Smith MV**, Klein SE, Clohisy JC, Baca GR, Brophy RH, Wright RW. Lower extremity-specific measures of disability and outcomes in orthopaedic surgery. *J Bone Joint Surg Am* 2012; **94**: 468-477 [PMID: 22398742 DOI: 10.2106/JBJS.J.01822]
- 23 **Beecher HK**. The powerful placebo. *J Am Med Assoc* 1955; **159**: 1602-1606 [PMID: 13271123 DOI: 10.1001/jama.1955.02960340022006]
- 24 **Freeman TB**, Vawter DE, Leaverton PE, Godbold JH, Hauser RA, Goetz CG, Olanow CW. Use of placebo surgery in controlled trials of a cellular-based therapy for Parkinson's disease. *N Engl J Med* 1999; **341**: 988-992 [PMID: 10498497 DOI: 10.1056/NEJM199909233411311]
- 25 **Wolf BR**, Buckwalter JA. Randomized surgical trials and "sham" surgery: relevance to modern orthopaedics and minimally invasive surgery. *Iowa Orthop J* 2006; **26**: 107-111 [PMID: 16789458]
- 26 **Bennell KL**, Egerton T, Martin J, Abbott JH, Metcalf B, McManus F, Sims K, Pua YH, Wrigley TV, Forbes A, Smith C, Harris A, Buchbinder R. Effect of physical therapy on pain and function in patients with hip osteoarthritis: a randomized clinical trial. *JAMA* 2014; **311**: 1987-1997 [PMID: 24846036 DOI: 10.1001/jama.2014.4591]
- 27 **Hall AM**, Ferreira PH, Maher CG, Latimer J, Ferreira ML. The influence of the therapist-patient relationship on treatment outcome in physical rehabilitation: a systematic review. *Phys Ther* 2010; **90**: 1099-1110 [PMID: 20576715 DOI: 10.2522/ptj.20090245]
- 28 **Jevsevar D**, Shea K, Cummins D, Murray J, Sanders J. Recent changes in the AAOS evidence-based clinical practice guidelines process. *J Bone Joint Surg Am* 2014; **96**: 1740-1741 [PMID: 25320201 DOI: 10.2106/JBJS.N.00658]
- 29 **Fergusson D**, Aaron SD, Guyatt G, Hébert P. Post-randomisation exclusions: the intention to treat principle and excluding patients from analysis. *BMJ* 2002; **325**: 652-654 [PMID: 12242181 DOI: 10.1136/bmj.325.7365.652]
- 30 **Gupta SK**. Intention-to-treat concept: A review. *Perspect Clin Res* 2011; **2**: 109-112 [PMID: 21897887 DOI: 10.4103/2229-3485.83221]
- 31 **Nagelkerke N**, Fidler V, Bernsen R, Borgdorff M. Estimating treatment effects in randomized clinical trials in the presence of non-compliance. *Stat Med* 2000; **19**: 1849-1864 [PMID: 10867675 DOI: 10.1002/sim.894]
- 32 **Sheiner LB**, Rubin DB. Intention-to-treat analysis and the goals of clinical trials. *Clin Pharmacol Ther* 1995; **57**: 6-15 [PMID: 7828382 DOI: 10.1016/0009-9236(95)90260-0]

P- Reviewer: Ohishi T S- Editor: Ji FF
L- Editor: A E- Editor: Liu SQ



Resection and reconstruction of pelvic and extremity soft tissue sarcomas with major vascular involvement: Current concepts

Niall P McGoldrick, Joseph S Butler, Maire Lavelle, Stephen Sheehan, Sean Dudeney, Gary C O'Toole

Niall P McGoldrick, Joseph S Butler, Sean Dudeney, Gary C O'Toole, National Sarcoma Service, Department of Trauma and Orthopaedic Surgery, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland

Maire Lavelle, Department of Histopathology, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland

Stephen Sheehan, Department of Vascular Surgery, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: The authors declare they have no potential conflicts of interest, nor have they received any financial support.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Niall P McGoldrick, MB, MCh, MRCSI, National Sarcoma Service, Department of Trauma and Orthopaedic Surgery, St Vincent's University Hospital, Merrion Rd, Elm Park, Dublin 4, Ireland. niallmcg@gmail.com
Telephone: +353-1-2214000
Fax: +353-1-2214001

Received: October 15, 2015

Peer-review started: October 18, 2015

First decision: January 4, 2016

Revised: February 16, 2016

Accepted: March 7, 2016

Article in press: March 9, 2016

Published online: May 18, 2016

Abstract

Soft tissue sarcoma accounts for approximately 1% of all cancers diagnosed annually in the United States. When these rare malignant mesodermal tumours arise in the pelvis and extremities, they may potentially encase or invade large calibre vascular structures. This presents a major challenge in terms of safe excision while also leaving acceptable surgical margins. In recent times, the trend has been towards limb salvage with vascular reconstruction in preference to amputation. Newer orthopaedic and vascular reconstructive techniques including both synthetic and autogenous graft reconstruction have made complex limb-salvage surgery feasible. Despite this, limb-salvage surgery with concomitant vascular reconstruction remains associated with higher rates of post-operative complications including infection and amputation. In this review we describe the initial presentation and investigation of patients presenting with soft tissue sarcomas in the pelvis and extremities, which involve vascular structures. We further discuss the key surgical reconstructive principles and techniques available for the management of these complex tumours, drawn from our institution's experience as a national tertiary referral sarcoma service.

Key words: Sarcoma; Extremities; Vascular surgical procedures; Limb salvage; Reconstruction

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This paper describes the investigation and management of patients presenting with a complex soft tissue pelvic and extremity sarcomas that also

compromise local vascular structures. The principles of surgical management of these cases are described in light of the most recent evidence, with examples drawn from our experience to illustrate these principles. We emphasize the importance of a multidisciplinary approach in the care of this complex patient cohort.

McGoldrick NP, Butler JS, Lavelle M, Sheehan S, Dudeney S, O'Toole GC. Resection and reconstruction of pelvic and extremity soft tissue sarcomas with major vascular involvement: Current concepts. *World J Orthop* 2016; 7(5): 293-300 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/293.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.293>

INTRODUCTION

Soft tissue sarcomas are rare malignant tumours that are invariably fatal if not treated aggressively. Surgical excision of these lesions offers the only hope of potential cure. Sarcomas located in the pelvis and extremities may potentially encase or invade large caliber vascular structures. This presents the orthopaedic surgeon with a major challenge in balancing safe excision while still maintaining acceptable surgical margins. Moreover, involvement of major vascular structures was historically assumed to carry grave prognosis, since it was thought the vessels would provide a route of haematogenous spread of the tumour^[1]. It was for this reason that early, more conservative attempts at limb preservation surgery, which frequently left inadequate margins, invariably resulted in unacceptably high rates of local recurrence.

The philosophical turning point in the management of these complex cases came with a report by Fortner *et al*^[2] describing the earliest initial series of *en bloc* resection of tumour with involved vascular structures. Although preservation of the limb was achieved, high rates of post-operative oedema were observed in patients where no vascular reconstruction was performed. Improved rates of oedema and function were observed in the subsequent three patients who underwent concomitant arterial reconstruction at the time of tumour resection by the same author.

Unsurprisingly given the nature and relative rarity of these aggressive tumours, no large randomized control trials investigating optimal treatment strategies have been reported in the literature. Issues surrounding the role of venous reconstruction, the choice of autologous vs synthetic graft, and appropriate anticoagulation have meant controversy remains concerning optimal treatment of this complex patient cohort. Despite this, technical advances in the fields of both orthopaedic and vascular surgery have resulted in a trend towards aggressive limb salvage with vascular reconstruction in preference to amputation. The addition of both pre- and post-operative radiotherapy and chemotherapy has resulted in a truly multimodal treatment strategy for

these complex cases.

The primary focus of this review will be to discuss the broad principles concerning the appropriate investigation and treatment of these complex tumours, with illustrative cases drawn from our institution's experience as a national tertiary referral center for sarcoma in Ireland. Particular attention will be paid to the strategy for management of the vascular component of these difficult resections.

EPIDEMIOLOGY AND PREVALENCE

Soft tissue sarcomas represent a heterogenous group of rare malignant tumours of mesenchymal origin with an estimated 9000 new cases diagnosed each year in the United States^[3]. Currently, more than 50 histological subtypes of soft tissue sarcoma have been characterized. More than half (59%) of these tumours are found in the extremities, although they may be found anywhere in the body^[4]. Despite improved treatment strategies, the overall survival rate for all stages of soft tissue sarcoma remains relatively disappointing at a level between 50% and 60%^[4]. Reports in the literature suggest involvement of adjacent blood vessels in approximately 5% of cases, although Schwarzbach *et al*^[5] report an incidence of 10%^[5,6].

INVESTIGATION

Clinical examination of the patient on initial presentation will often elicit the possibility of vascular involvement of a sarcomatous lesion. Reduced or absent palpable arterial pulsation distal to the level of a mass should raise concern in the clinician's mind about vascular compromise.

Magnetic resonance imaging (MRI) has now become the gold standard of work-up for soft tissue sarcoma and should be performed to evaluate any suspicious lesions. However, colour duplex sonography, computed tomography (CT) and formal angiography have all been reported modalities used in the diagnosis of a soft tissue sarcoma invading vascular structures^[5,7-9]. The addition of radiographic contrast to the study helps delineate vascular structures. The location of the mass, its depth in relation to fascia, heterogeneity and signal characteristics should be determined. More specifically, the relationship of the lesion to adjacent blood vessels, and other important structures, must carefully be considered. Vascular involvement may be diagnosed when MRI or CT demonstrates absence of normal tissue in the tumour-to-vessel plane^[5]. MRI and magnetic resonance imaging angiography (MRA) can be useful in guiding the surgeon as to the length of vessel that is likely to be resected, as well as identifying potential donor vessels for reconstruction. Pre-operatively, lower limb venous duplex and vein marking of the contralateral limb may also be useful to map patent vein graft available for harvest at the time of resection.

All of these factors should be weighed-up by the

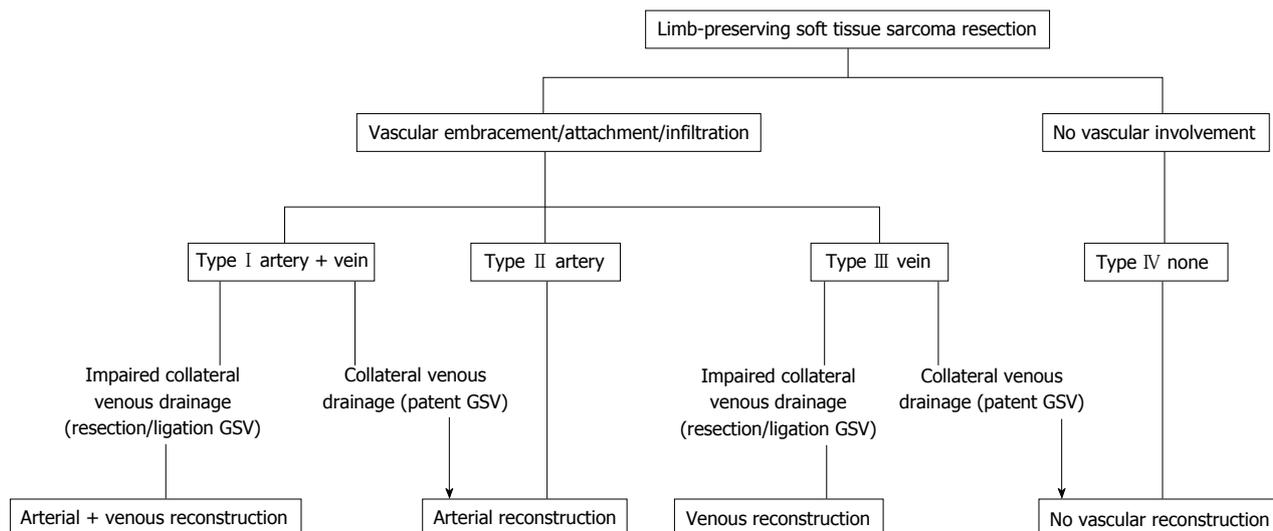


Figure 1 Types of vascular involvement by soft tissue sarcomas of the extremity and algorithm for reconstructive options (adapted from, with permission of Elsevier from Schwarzbach *et al*^[5]). GSV: Great saphenous vein.

operating surgeon in planning any proposed attempt at surgical resection. Involvement of a vascular surgeon at this point, where there exists the possibility of major vessel reconstruction, is crucial.

CLASSIFICATION OF VASCULAR INVOLVEMENT

Schwarzbach *et al*^[5] have classified the pattern of vascular involvement, which may be useful in guiding surgical management (Figure 1). Type I soft tissue sarcomas involve both major arteries and veins, while Type II lesions involve the artery in isolation. Type III lesions were characterized as those with purely venous involvement, leaving an intact artery. Type IV lesions have no involvement of either artery or vein, and require no vascular reconstruction.

In cases of type I involvement, Schwarzbach *et al*^[5] propose both arterial and venous reconstruction where there is impaired collateral venous drainage. In type I cases with adequate venous drainage, arterial reconstruction alone may be sufficient.

In type II cases, the artery may be resected, and reconstructed using either venous autograft or alternatively prosthetic material, depending on surgeon preference and available autogenous graft. Some authors have advocated the use of isolated limb perfusion in these cases^[10,11]. The rationale for this is to isolate the limb from circulation to facilitate direct administration of high dose cytotoxic agents, with the aim of down-staging the tumour, and ultimately preserving the native vascular structures. The role of this modality of treatment, however, remains controversial.

In type III cases, venous reconstruction has been advocated where there is impaired venous drainage. If sufficient venous drainage does exist, then type III cases may be treated as type IV cases, with resection

of the lesion alone.

GENERAL PRINCIPLES OF SURGICAL TECHNIQUE

A number of general principles governing resection of these complex lesions may be elicited from the literature. A multidisciplinary team should be considered mandatory for successful limb salvage in these cases. This involves not only the orthopaedic and vascular surgeons but also allied health professionals including physiotherapists, dieticians and occupational therapists. Resections should only be performed in a specialized tertiary-level institution with both orthopaedic and vascular surgical services familiar with the management of complex soft tissue sarcomas. Radiological and theatre departments should have angiographic capabilities on site. Additionally, plastic and reconstructive surgery may be necessitated by the nature and size of tissue resected, and thus access to this specialty should be easily available if required.

The required volume of tissue that the operating surgeon must resect to ensure an adequate and wide margin can be determined by the tissue surrounding the lesion. Fascia is considered impenetrable to tumour cells, and thus may act as a margin in its own right. However, skin, fat and muscle are easily penetrated and thus 2-3 cm of these tissues must be excised^[12].

Difficulty arises when determining safe margins where major vessels are in the surgical field. Inevitably, a major vessel must be sacrificed if tumour originates within the lumen of the vessel itself^[5]. Where tumour surrounds a vessel, or infiltrates its wall, resection of the vessel may also become necessary^[5,13].

The adventitial layer of the vessel may be considered an acceptable margin. Some authors have advocated longitudinal division of the adventitia on the side oppo-

site to the tumour^[5,14-16]. The layer is opened like a book, allowing the vessel to be mobilized and released. Moreover, patch-type reconstructions may be an option where tumour is in very limited contact with the vessel wall^[12]. Cipriano *et al*^[12] note that the pseudocapsule that typically surrounds soft tissue sarcomas should not be considered equivalent to fascia, and should be treated as a contaminated plane.

The initial strategy in these procedures is to mobilise the tumour, while controlling and preserving vascular structures proximal and distal to the lesion^[15]. As with all tumour surgery, one of the primary goals is to prevent contamination of the surgical bed by tumour cells. For this reason, Matsumoto *et al*^[17] introduced the concept of complete isolation of the tumour mass once mobilized using a vinyl sheet, drape or gauze. Attention must then turn to the careful dissection of adjacent or involved vascular structures.

Ischaemic time of the limb must be a consideration throughout the procedure. Vessel clamping and division should be performed just prior to complete excision of the tumour. Baxter *et al*^[18] suggest the administration of 50 units/kg of heparin 5 min prior to the application of clamps. Emori *et al*^[8] administered 1 mg/kg of heparin immediately prior to clamping. In their series, Muramatsu *et al*^[19] preferred the administration of 2000-5000 U of intravenous heparin immediately following vascular anastomosis. Following complete division of the vessels and final excision of the tumour mass, arterial and venous shunts may also be placed to reduce ischaemic time. The routine lowering of ambient room temperature in the operating theatre at the time of vascular reconstruction has also been reported^[19].

Once the tumour mass has been excised, with control of compromised vessels, attention must then turn to vascular reconstruction. A number of vascular reconstructive options are available to the surgeon, and the choice of specific graft depends on the length and caliber of vessel required, the availability of suitable venous graft in the contralateral limb, and surgeon experience and preference. Options variously described in the literature include contralateral superficial femoral vein graft, reversed long saphenous vein graft, or synthetic grafts such as polytetrafluoroethylene or polyethylene terephthalate^[5,7,8,15,18-22].

Routinely patients should receive prophylactic antibiotic treatment, and a closed suction drain may also be placed at time of closure. In the post-operative setting, follow-up should be as standard for soft tissue sarcoma resections. However, additionally the patency of vascular anastomoses should be followed at regular intervals.

CONTROVERSIES IN MANAGEMENT

It should be noted that while limb salvage is possible, the precise manner in which this is achieved has been variously described. Given the nature of the pathology, large randomized control trials would be both difficult

to construct and ethically inappropriate. As such, there is some controversy in the literature regarding some aspects of treatment of this patient cohort. In particular, the optimal choice of substitute vessel graft is not well established, and whether venous reconstruction is necessary also remains unclear.

Arterial reconstruction following resection is clearly indicated since the limb is unlikely to survive due to the high risk of ischaemia. Evidence in the literature favouring similarly aggressive venous reconstruction is less robust. Fortner *et al*^[2] and Imparato *et al*^[23] report some of the earliest experiences of venous reconstruction. In general terms, however, reports of venous reconstruction in the literature are less frequently encountered. Moreover, in those reports where venous reconstruction was performed, follow-up data is occasionally absent and difficult to interpret^[6,23,24].

Patients undergoing venous resection without reconstruction have been observed to experience post-operative oedema, discoloration of the limb and venous eczema^[22,25]. Some authors have described successful management of oedema through use of simple elevation and elastic support^[6,23]. Additionally, it has been argued that limb oedema may be more reflective of lymphatic disruption than venous deficiency^[26]. Furthermore, both Tsukushi *et al*^[27] and Adelani *et al*^[28] have found no reduction in post-operative oedema when venous reconstruction was performed.

Despite these observations, a majority of reports describe attempts made by surgeons to reconstruct the venous system in every case, or at least in those cases where sufficient concern exists for collateral flow^[5,7,8,18,19,21]. It may well be that the rate of post-operative oedema correlates closely with the degree of disruption of venous collaterals at the time of surgical resection.

Concerning the specific choice of material for vascular reconstructions, there appears to be no clear evidence supporting one material over another. Both autologous vein and prosthetic material have been used successfully (Table 1). Some authors have preferred the use of autologous material in preference to prosthetic graft^[5,22,29].

The great saphenous vein remains a common and popular choice of graft for both arterial and venous reconstructions. Its length and diameter is generally amenable to use as a vascular conduit, and it is easily accessible for harvest at the time of operation. Further, saphenous vein graft has been reported to afford superior patency rates at four years when compared with prosthetic graft (68% vs 38%)^[30]. There is not universal agreement on this point, and other reports suggest that there is no superior advantage to autologous graft over synthetic graft in terms of patency in the longer term^[2,23,31].

Against these observations, it has been argued that saphenous graft may be of inadequate length for reconstructive purposes, and harvest carries additional

Table 1 Venous grafts and patency rates

Ref.	Number (<i>n</i>)	Graft material (<i>n</i>)	Patency
Imparato <i>et al</i> ^[23]	3	Saphenous	
Nambisan <i>et al</i> ^[35]	6	PTFE	33%
Steed <i>et al</i> ^[36]	1	Saphenous	
Karakousis <i>et al</i> ^[37]	9	PTFE	0%
Kawai <i>et al</i> ^[26]	7	PTFE (5), saphenous (2)	14%
Kopera <i>et al</i> ^[29]	13	Saphenous (8), PTFE (4), PETE (1)	77%
Karakousis <i>et al</i> ^[6]	15	PTFE (14), saphenous (1)	
Hohenberger <i>et al</i> ^[13]	10	Saphenous (6), PTFE (4)	72%
Bonardelli <i>et al</i> ^[14]	5	Saphenous (3), transposition (2)	100%
Leggon <i>et al</i> ^[24]	8	Saphenous (5), femoral (2), PETE (1)	
Schwarzbach <i>et al</i> ^[5]	12	PTFE (10), saphenous (2)	58%
Nishinari <i>et al</i> ^[22]	17	Saphenous (12), PTFE (3), PETE (2)	82%
Song <i>et al</i> ^[21]	9	Saphenous (4), femoral vein (2), Allograft (3)	78%
López-Anglada Fernández <i>et al</i> ^[15]	1	PTFE (1)	100%
Muramatsu <i>et al</i> ^[19]	12	Saphenous (10), PTFE (2)	
Emori <i>et al</i> ^[8]	9	PTFE (9)	
Viñals Viñals <i>et al</i> ^[38]	1	Saphenous (1)	100%
Umezawa <i>et al</i> ^[7]	13	Saphenous (13)	

PTFE: Polytetrafluoroethylene; PETE: Polyethylene terephthalate.

morbidity in terms of longer operative time, and additional surgical exposure and wounds. Regardless of the material chosen, it should be of sufficient length and caliber to appropriately and securely reconstruct the resected vessel.

POST-OPERATIVE FUNCTION

Limb salvage surgery should seek to leave the patient with a limb which functions superiorly when compared with amputation and prosthetic replacement. This should not be at the expense of oncological outcome^[12]. The literature has relatively few reports concerning the functional outcomes of those patients undergoing limb-salvage surgery with concomitant vascular reconstruction. In one report of pooled data, 76% of a cohort of 58 patients for whom functional outcome measures were available reported having a "functional limb"^[24].

Wound complications, tumour size and motor nerve sacrifice have been identified as determinants of overall functional outcome after limb-salvage surgery and radiotherapy for soft tissue sarcoma^[32,33]. Ghert *et al*^[20] matched each of a cohort of patients undergoing limb salvage and vascular reconstruction with two other patients not undergoing vascular reconstruction, on the basis of tumour size, wound complications and pre-operative toronto extremity salvage score (TESS) score. The TESS score is a functional measure of physical disability, specifically designed for patients with extremity sarcoma^[34]. At one year post-operatively, those patients undergoing vascular reconstruction had only slightly lower post-operative TESS scores.

Schwarzbach *et al*^[5] found that of nine patients interviewed regarding limb function, five reported their outcome as excellent, three felt their outcome was good, while one patient reported a poor outcome due to contracture.

SURVIVAL AND RECURRENCE

It is possible to obtain reasonably good survival rates with careful pre-operative planning and appropriate and timely intervention. Recurrence of tumour remains an issue however. Schwarzbach *et al*^[5] report recurrence in 15.8% (*n* = 3) of 19 patients in their study. A slightly higher figure of 21% has been reported by Song *et al*^[21].

Two-year survival has been variously reported in the literature, ranging from 58.6% to 70.4%^[5,8,22]. At five years post surgery, approximately one in two patients will have died from their disease, with reported figures ranging from 42.4% to 70%^[5,8,21,22].

ILLUSTRATIVE CASES

Case 1

A 73-year-old woman presented with a high grade, stage III leiomyosarcoma in her left inguinal region. The lesion was present for approximately one year prior to presentation and measured 11 centimeters in maximum diameter. CT and MRI demonstrated a large tumour mass invading the left common femoral vein, and surrounded the anterior aspect of the common femoral artery for greater than 180 degrees of the vessel surface. The tumour mass was intimately related to adjacent vessels and was found to interdigitate the common femoral bifurcation (Figure 2). The lesion was resected *en-bloc* with concomitant vascular reconstruction (Figure 3). Arterial reconstruction involved an end-to-end anastomosis from the external iliac artery to superficial femoral artery using an 8-millimetre Gortex synthetic graft. The contralateral long saphenous vein was harvested for venous reconstruction. An end-to-end anastomosis between the superficial femoral vein and external iliac vein was performed.



Figure 2 Axial cut computed tomography angiogram demonstrating proximity of a soft tissue sarcoma to the adjacent femoral vessels (arrow).



Figure 3 Completed vascular reconstruction following excision of lesion.



Figure 4 Antero-lateral projection of reconstructed magnetic resonance angiogram of left proximal calf demonstrating the tumour mass in relation to adjacent vascular structures.



Figure 5 Histopathological specimen of tumour adjacent to vessel.

Post-operatively, the patient’s wound healed without complication. In view of the necessary vascular reconstruction, anti-coagulation with warfarin was commenced. At one month post-operatively however, she required ileo-femoral-popliteal thrombectomy for graft thrombosis. The patient completed a course of adjuvant radiotherapy to the tumour bed (66 Gy in 33 fractions).

Case 2

A 16-year-old young woman presented to clinic with a 5-year history of progressive swelling in her left calf. Multi-modality investigations including CT angiogram, MRI and MRA, and tissue biopsy confirmed a 4.2 cm × 5.6 cm × 7.2 cm hypervascular and heterogenous mass, with features of central necrosis, in the posterior compartment of the upper calf (Figure 4). The tumour mass was found to lie in the neurovascular plain, with multiple vessels feeding from the peroneal and posterior tibial arteries. The anterior tibial artery was uninvolved. Microscopy confirmed an alveolar soft part sarcoma.

The surgical strategy involved pre-operative embolization of the feeder vessels as described. The following day, the tumour mass was resected *en-bloc* with concomitant vascular reconstruction. Popliteal and anterior tibial vessels were preserved. Peroneal and posterior

tibial vessels were resected with tumour. The posterior tibial artery was revascularized from approximately 5 cm beyond its origin mid-calf using a reversed long saphenous vein graft harvested from the contralateral leg. Anastomosis was performed in an end-to-end fashion.

At the time of diagnosis, the patient was found to have lung metastases. She underwent adjuvant chemotherapy and radiotherapy to both lungs (19.5 Gy in 13 fractions) and to the tumour bed (50.4 Gy in 28 fractions). At 48 mo follow-up, the patient was well without further complications.

Case 3

A 56-year-old man presented with a 2-mo history of painless swelling in the right popliteal fossa. He had a history of having lentigo maligna excised from his ear some 5 mo earlier, but was otherwise healthy. MRI and MRA revealed a large soft tissue mass in the superior popliteal fossa measuring 8.5 cm × 7.8 cm × 4.5 cm in dimension. The tumour encased the popliteal artery for at least 270 degrees of its circumference over a distance of 8 cm (Figure 5). Subsequent biopsy revealed grade II stage I B leiomyosarcoma.

The patient received pre-operative radiotherapy (50 Gy in 25 fractions) before definitive surgical resection. Arterial reconstruction required reverse long saphenous vein graft with end-to-end anastomosis. Venous recon-

struction was not necessary. Post-operatively, there were no major vascular complications.

CONCLUSION

Patients presenting with soft tissue sarcomas that involve major vascular structures represent a unique and complex cohort of patients. Advances in both orthopaedic and vascular surgery have made it possible to successfully resect these lesions and achieve limb-salvage while also maintaining reasonable function. A multidisciplinary approach with careful pre-operative evaluation is essential to improve outcome.

ACKNOWLEDGMENTS

The authors would like to thank Professor, Dr. med. Matthias Schwarzbach and Elsevier for kindly allowing us to use Figure 1 in the text.

REFERENCES

- Ruka W**, Emrich LJ, Driscoll DL, Karakousis CP. Prognostic significance of lymph node metastasis and bone, major vessel, or nerve involvement in adults with high-grade soft tissue sarcomas. *Cancer* 1988; **62**: 999-1006 [PMID: 3409181 DOI: 10.1002/1097-0142(19880901)62:5<999::AID-CNCR2820620527>3.0.CO;2-N]
- Fortner JG**, Kim DK, Shiu MH. Limb-preserving vascular surgery for malignant tumors of the lower extremity. *Arch Surg* 1977; **112**: 391-394 [PMID: 849146 DOI: 10.1001/archsurg.1977.01370040043007]
- Gilbert NF**, Cannon CP, Lin PP, Lewis VO. Soft-tissue sarcoma. *J Am Acad Orthop Surg* 2009; **17**: 40-47 [PMID: 19136426 DOI: 10.5435/00124635-200901000-00006]
- Cormier JN**, Pollock RE. Soft tissue sarcomas. *CA Cancer J Clin* 2004; **54**: 94-109 [PMID: 15061599 DOI: 10.3322/canjclin.54.2.94]
- Schwarzbach MH**, Hormann Y, Hinz U, Bernd L, Willeke F, Mechttersheimer G, Böckler D, Schumacher H, Herfarth C, Büchler MW, Allenberg JR. Results of limb-sparing surgery with vascular replacement for soft tissue sarcoma in the lower extremity. *J Vasc Surg* 2005; **42**: 88-97 [PMID: 16012457 DOI: 10.1016/j.jvs.2005.03.017]
- Karakousis CP**, Karpaliotis C, Driscoll DL. Major vessel resection during limb-preserving surgery for soft tissue sarcomas. *World J Surg* 1996; **20**: 345-349; discussion 350 [PMID: 8661843 DOI: 10.1007/s002689900056]
- Umezawa H**, Sakuraba M, Miyamoto S, Nagamatsu S, Kayano S, Taji M. Analysis of immediate vascular reconstruction for lower-limb salvage in patients with lower-limb bone and soft-tissue sarcoma. *J Plast Reconstr Aesthet Surg* 2013; **66**: 608-616 [PMID: 23391538 DOI: 10.1016/j.bjps.2013.01.001]
- Emori M**, Hamada K, Omori S, Joyama S, Tomita Y, Hashimoto N, Takami H, Naka N, Yoshikawa H, Araki N. Surgery with vascular reconstruction for soft-tissue sarcomas in the inguinal region: oncologic and functional outcomes. *Ann Vasc Surg* 2012; **26**: 693-699 [PMID: 22664282 DOI: 10.1016/j.avsg.2011.12.003]
- Bains R**, Magdum A, Bhat W, Roy A, Platt A, Stanley P. Soft tissue sarcoma - A review of presentation, management and outcomes in 110 patients. *Surgeon* 2014; Epub ahead of print [PMID: 25261278 DOI: 10.1016/j.surge.2014.06.002]
- Eggermont AM**, Schraffordt Koops H, Klausner JM, Kroon BB, Schlag PM, Liénard D, van Geel AN, Hoekstra HJ, Meller I, Nieweg OE, Kettelhack C, Ben-Ari G, Pector JC, Lejeune FJ. Isolated limb perfusion with tumor necrosis factor and melphalan for limb salvage in 186 patients with locally advanced soft tissue extremity sarcomas. The cumulative multicenter European experience. *Ann Surg* 1996; **224**: 756-764; discussion 764-765 [PMID: 8968230 DOI: 10.1097/0000658-199612000-00011]
- Wray CJ**, Benjamin RS, Hunt KK, Cormier JN, Ross MI, Feig BW. Isolated limb perfusion for unresectable extremity sarcoma: results of 2 single-institution phase 2 trials. *Cancer* 2011; **117**: 3235-3241 [PMID: 21246524 DOI: 10.1002/cncr.25850]
- Cipriano CA**, Wunder JS, Ferguson PC. Surgical Management of Soft Tissue Sarcomas of the Extremities. *Oper Tech Orthop* 2014; **24**: 79-84 [DOI: 10.1053/j.oto.2014.02.010]
- Hohenberger P**, Allenberg JR, Schlag PM, Reichardt P. Results of surgery and multimodal therapy for patients with soft tissue sarcoma invading to vascular structures. *Cancer* 1999; **85**: 396-408 [PMID: 10023708 DOI: 10.1002/(SICI)1097-0142(19990115)85:2<396::AID-CNCR18>3.0.CO;2-O]
- Bonardelli S**, Nodari F, Maffei R, Ippolito V, Saccalani M, Lussardi L, Giulini S. Limb salvage in lower-extremity sarcomas and technical details about vascular reconstruction. *J Orthop Sci* 2000; **5**: 555-560 [PMID: 11180918 DOI: 10.1007/s007760070005]
- López-Anglada Fernández E**, Rubio Sanz J, Braña Vigil A. Vascular reconstruction during limb preserving surgery in the treatment of lower limb sarcoma: A report on four cases. *Rev Esp Cir Ortop Traumatol* 2009; **53**: 386-393 [DOI: 10.1016/s1988-8856(09)70199-3]
- Ceraldi CM**, Wang TN, O'Donnell RJ, McDonald PT, Granelli SG. Vascular reconstruction in the resection of soft tissue sarcoma. *Perspect Vasc Surg* 2000; **12**: 67-83 [DOI: 10.1177/153100350001200214]
- Matsumoto S**, Kawaguchi N, Manabe J, Matsushita Y. "In situ preparation": new surgical procedure indicated for soft-tissue sarcoma of a lower limb in close proximity to major neurovascular structures. *Int J Clin Oncol* 2002; **7**: 51-56 [PMID: 11942050]
- Baxter BT**, Mahoney C, Johnson PJ, Selmer KM, Pipinos II, Rose J, Neff JR. Concomitant arterial and venous reconstruction with resection of lower extremity sarcomas. *Ann Vasc Surg* 2007; **21**: 272-279 [PMID: 17484959 DOI: 10.1016/j.avsg.2007.03.005]
- Muramatsu K**, Ihara K, Miyoshi T, Yoshida K, Taguchi T. Clinical outcome of limb-salvage surgery after wide resection of sarcoma and femoral vessel reconstruction. *Ann Vasc Surg* 2011; **25**: 1070-1077 [PMID: 21831587 DOI: 10.1016/j.avsg.2011.05.009]
- Ghert MA**, Davis AM, Griffin AM, Alyami AH, White L, Kandel RA, Ferguson P, O'Sullivan B, Catton CN, Lindsay T, Rubin B, Bell RS, Wunder JS. The surgical and functional outcome of limb-salvage surgery with vascular reconstruction for soft tissue sarcoma of the extremity. *Ann Surg Oncol* 2005; **12**: 1102-1110 [PMID: 16252136 DOI: 10.1245/ASO.2005.06.036]
- Song TK**, Harris EJ, Raghavan S, Norton JA. Major blood vessel reconstruction during sarcoma surgery. *Arch Surg* 2009; **144**: 817-822 [PMID: 19797105 DOI: 10.1001/archsurg.2009.149]
- Nishinari K**, Wolosker N, Yazbek G, Zerati AE, Nishimoto IN. Venous reconstructions in lower limbs associated with resection of malignancies. *J Vasc Surg* 2006; **44**: 1046-1050 [PMID: 17098540 DOI: 10.1016/j.jvs.2006.07.033]
- Imparato AM**, Roses DF, Francis KC, Lewis MM. Major vascular reconstruction for limb salvage in patients with soft tissue and skeletal sarcomas of the extremities. *Surg Gynecol Obstet* 1978; **147**: 891-896 [PMID: 280963]
- Leggon RE**, Huber TS, Scarborough MT. Limb salvage surgery with vascular reconstruction. *Clin Orthop Relat Res* 2001; **(387)**: 207-216 [PMID: 11400886 DOI: 10.1097/00003086-200106000-00028]
- Matsushita M**, Kuzuya A, Mano N, Nishikimi N, Sakurai T, Nimura Y, Sugiura H. Sequelae after limb-sparing surgery with major vascular resection for tumor of the lower extremity. *J Vasc Surg* 2001; **33**: 694-699 [PMID: 11296319 DOI: 10.1067/mva.2001.112799]
- Kawai A**, Hashizume H, Inoue H, Uchida H, Sano S. Vascular reconstruction in limb salvage operations for soft tissue tumors of the extremities. *Clin Orthop Relat Res* 1996; **(332)**: 215-222 [PMID: 8913166 DOI: 10.1097/00003086-199611000-00029]
- Tsukushi S**, Nishida Y, Sugiura H, Nakashima H, Ishiguro N. Results of limb-salvage surgery with vascular reconstruction for

- soft tissue sarcoma in the lower extremity: comparison between only arterial and arterovenous reconstruction. *J Surg Oncol* 2008; **97**: 216-220 [PMID: 18161869 DOI: 10.1002/jso.20945]
- 28 **Adelani MA**, Holt GE, Dittus RS, Passman MA, Schwartz HS. Revascularization after segmental resection of lower extremity soft tissue sarcomas. *J Surg Oncol* 2007; **95**: 455-460 [PMID: 17458861 DOI: 10.1002/jso.20679]
- 29 **Koperna T**, Teleky B, Vogl S, Windhager R, Kainberger F, Schatz KD, Kotz R, Polterauer P. Vascular reconstruction for limb salvage in sarcoma of the lower extremity. *Arch Surg* 1996; **131**: 1103-1107; discussion 1108 [PMID: 8857912 DOI: 10.1001/archsurg.1996.01430220097023]
- 30 **Veith FJ**, Gupta SK, Ascer E, White-Flores S, Samson RH, Scher LA, Towne JB, Bernhard VM, Bonier P, Flinn WR. Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. *J Vasc Surg* 1986; **3**: 104-114 [PMID: 3510323 DOI: 10.1016/0741-5214(86)90073-X]
- 31 **Wuisman P**, Grunert J. [Blood vessel transfer allowing avoidance of surgical rotation or amputation in the management of primary malignant tumors of the knee]. *Rev Chir Orthop Reparatrice Appar Mot* 1994; **80**: 720-727 [PMID: 7638401]
- 32 **Davis AM**, O'Sullivan B, Bell RS, Turcotte R, Catton CN, Wunder JS, Chabot P, Hammond A, Benk V, Isler M, Freeman C, Goddard K, Bezjak A, Kandel RA, Sadura A, Day A, James K, Tu D, Pater J, Zee B. Function and health status outcomes in a randomized trial comparing preoperative and postoperative radiotherapy in extremity soft tissue sarcoma. *J Clin Oncol* 2002; **20**: 4472-4477 [PMID: 12431971 DOI: 10.1200/JCO.2002.03.084]
- 33 **Davis AM**, Sennik S, Griffin AM, Wunder JS, O'Sullivan B, Catton CN, Bell RS. Predictors of functional outcomes following limb salvage surgery for lower-extremity soft tissue sarcoma. *J Surg Oncol* 2000; **73**: 206-211 [PMID: 10797333 DOI: 10.1002/(SICI)1096-9098(200004)73:4<206::AID-JSO4>3.0.CO;2-5]
- 34 **Davis AM**, Wright JG, Williams JI, Bombardier C, Griffin A, Bell RS. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual Life Res* 1996; **5**: 508-516 [PMID: 8973131 DOI: 10.1007/BF00540024]
- 35 **Nambisan RN**, Karakousis CP. Vascular reconstruction for limb salvage in soft tissue sarcomas. *Surgery* 1987; **101**: 668-677 [PMID: 3589963]
- 36 **Steed DL**, Peitzman AB, Webster MW, Ramasastry SS, Goodman MA. Limb sparing operations for sarcomas of the extremities involving critical arterial circulation. *Surg Gynecol Obstet* 1987; **164**: 493-498 [PMID: 3473704]
- 37 **Karakousis CP**, Emrich LJ, Vesper DS. Soft-tissue sarcomas of the proximal lower extremity. *Arch Surg* 1989; **124**: 1297-1300 [PMID: 2818184 DOI: 10.1001/archsurg.1989.01410110055011]
- 38 **Viñals Viñals JM**, Gomes Rodrigues TA, Perez Sidelnikova D, Serra Payro JM, Palacin Porté JA, Higuera Suñe C. [Vascular reconstruction for limb preservation during sarcoma surgery: a case series and a management algorithm]. *Rev Esp Cir Ortop Traumatol* 2013; **57**: 21-26 [PMID: 23594979 DOI: 10.1016/j.recot.2012.08.005]

P- Reviewer: de Bree E, Sakamoto A, Ueda H **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Liu SQ



Valgus osteotomy for nonunion and neglected neck of femur fractures

Viju Daniel Varghese, Abel Livingston, P R Boopalan, Thilak S Jepeganam

Viju Daniel Varghese, Abel Livingston, P R Boopalan, Thilak S Jepeganam, Department of Orthopaedics-Unit 3, Christian Medical College, Vellore 632004, Tamil Nadu, India

Author contributions: Jepeganam TS conceived of and designed the study, performed all the analysis, and wrote the manuscript; all authors contributed to this manuscript.

Conflict-of-interest statement: The author has no interests, commercial or otherwise, which represent a conflict of interest in relation to this study.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Thilak S Jepeganam, Professor, Department of Orthopaedics-Unit 3, Christian Medical College, Ida Scudder Road, Vellore 632004, Tamil Nadu, India. thilakjepeganam@yahoo.com
Telephone: +91-416-2282091
Fax: +91-416-2232035

Received: October 24, 2015
Peer-review started: December 9, 2015
First decision: January 4, 2016
Revised: February 2, 2016
Accepted: February 23, 2016
Article in press: February 24, 2016
Published online: May 18, 2016

Abstract

Nonunion neck of femur can be a difficult problem to treat, particularly in the young, and is associated with high complication rates of avascular necrosis due to the precarious blood supply and poor biomechanics.

The various treatment options that have been described can be broadly divided according to the aim of improving either biology or biomechanics. Surgeries aimed at improving the biology, such as vascularized fibula grafting, have good success rates but require high levels of expertise and substantial resources. A popular surgical treatment aimed at improving the biomechanics-valgus intertrochanteric osteotomy-optimizes conditions for fracture healing by converting shear forces across the fracture site into compressive forces. Numerous variations of this surgical procedure have been developed and successfully applied in clinical practice. As a result, the proximal femoral orientation for obtaining a good functional outcome has evolved over the years, and the present concept of altering the proximal femoral anatomy as little as possible has arisen. This technical objective supports attaining union as well as a good functional outcome, since excessive valgus can lead to increased joint reaction forces. This review summarizes the historical and current literature on valgus intertrochanteric osteotomy treatment of nonunion neck of femur, with a focus on factors predictive of good functional outcome and potential pitfalls to be avoided as well as controversies surrounding this procedure.

Key words: Neck of femur; Valgus intertrochanteric osteotomy; Head shaft angle; Neck resorption ratio; Nonunion

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Valgus intertrochanteric osteotomy is a viable treatment option for nonunion neck of femur. Size of the proximal fragment appears to be a significant predictive factor of fracture union. While valgus orientation of the proximal femur is important for fracture union, excessive valgus can lead to a poor functional outcome. The neck resorption ratio may be useful for measuring the proximal fragment and the head shaft angle may be

useful for studying proximal femoral alignment in the presence of neck resorption.

Varghese VD, Livingston A, Boopalan PR, Jepeganalam TS. Valgus osteotomy for nonunion and neglected neck of femur fractures. *World J Orthop* 2016; 7(5): 301-307 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/301.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.301>

INTRODUCTION

Nonunion neck of femur (NOF) fracture remains a significant challenge to treating orthopedists in the 21st century. Indeed, some studies have shown the nonunion rate to be as high as 30%^[1-3]. Nonunion following surgical fixation can result from initial fracture displacement, poor fracture reduction, or fixation in fractures with posterior comminution^[4-6]. Neglected NOF fractures are more commonly seen in the developing world^[7] and are associated with a particular profile of complications that includes osteopenia, resorption of neck, and avascular necrosis (AVN)^[4-6]; unfortunately, these complications are also further detrimental to head salvage. The methods of treating nonunion aim either at improving the biology and bone stock (*i.e.*, non vascularized and vascularized bone grafts^[7,8], muscle pedicle graft)^[9] or improving the biomechanics (*i.e.*, valgus osteotomy)^[10,11].

The concept of valgus osteotomy was refined by Pauwels^[6] in 1927, according to his findings showing that nonunion NOF was due to the high shear forces that increased with the vertical orientation of the fracture. The proposed biomechanical solution was to redirect these forces into compression forces *via* an angulation osteotomy and fixation with a blade plate device. Valgus intertrochanteric osteotomy as described by Pauwels^[6] and subsequently modified by Muller^[12] is still in use today, and remains a popular treatment option as it has a high success rate and corrects the common symptoms of coxa vara and associated limb length discrepancy^[11-14]. Marti *et al*^[10] helped to popularize the valgus intertrochanteric osteotomy for nonunion NOF by reporting good outcome in a long-term follow-up study.

This review provides a summary of the historical and most up-to-date literature on the valgus intertrochanteric osteotomy for nonunion NOF, detailing the underlying philosophy and technical principles of the procedure and discussing its most common and potential complications, with the aim of helping practicing orthopedists to understand the most relevant concepts that may improve rates of good functional outcome.

OPERATIVE PROCEDURE

The operative procedure is a modification of the method described by Muller^[12].

Step 1: Preoperative templating

Templating, performed on the normal hip, provides information for the position of the implant and size of the wedge (Figure 1A). The angle that the fracture line makes with the horizontal should be measured. The angle of wedge measured for removal in the intertrochanteric region is necessary to ensure the vertical fracture plane achieves a near-physiological orientation. However, this angle may be difficult to calculate in patients with long-standing nonunion and can only be confirmed when a closed reduction is obtained on the fracture table^[14]. Another complicating factor is that the neck in these patients is often resorbed on the inferior and posterior aspect, which can cause retroversion when impacting the fracture during fixation.

Step 2: Reduction and stabilization

Closed reduction in case of nonunion or neglected fracture would be difficult and should be attempted on the fracture table. Excessive traction to attempt a closed reduction should be avoided as this may stretch and injure the retinaculum, which is less mobile because of surrounding scar tissue. In our experience, the proximal fragment will occasionally have an inferior spike that prevents reduction and requires osteotomization to achieve acceptable alignment. Open reduction should be attempted only if deemed essential as further dissection could damage the precarious blood supply to the femoral head. Once the reduction is maintained with K-wire, the fracture is stabilized with a screw plate or a blade plate device (Figure 1B).

Step 3: Osteotomy and fixation

A lateral closing wedge is taken from the intertrochanteric region, after which the osteotomy is closed by clamping the plate to the bone. While the calculated wedge may be as high as 40 degrees, most authors in the recent literature have reported that a wedge of 25-30 degrees is often sufficient to produce the desired effect^[11,14,15]. Even in cases where an osteotomy is not required to obtain a valgus orientation, its advisable to do so as, this may help improve the blood supply to the femoral head. Compression across the fracture site can be achieved with a sliding hip screw, according to the intrinsic nature of the screw itself. However, when a double-angled blade plate device is applied, it is recommended that the length of the blade be 5-10 mm shorter than the measurement value. Firm impaction when inserting the blade plate helps to ensure that compression is obtained across the fracture site (Figure 1C and D). It is our opinion that this impaction is the most important factor in attaining union.

POTENTIAL PITFALLS

Excessive valgus orientation

Often the calculated angle to convert a Pauwels 3 to Pauwels 1 may be as high as 40-50 degrees. Removal

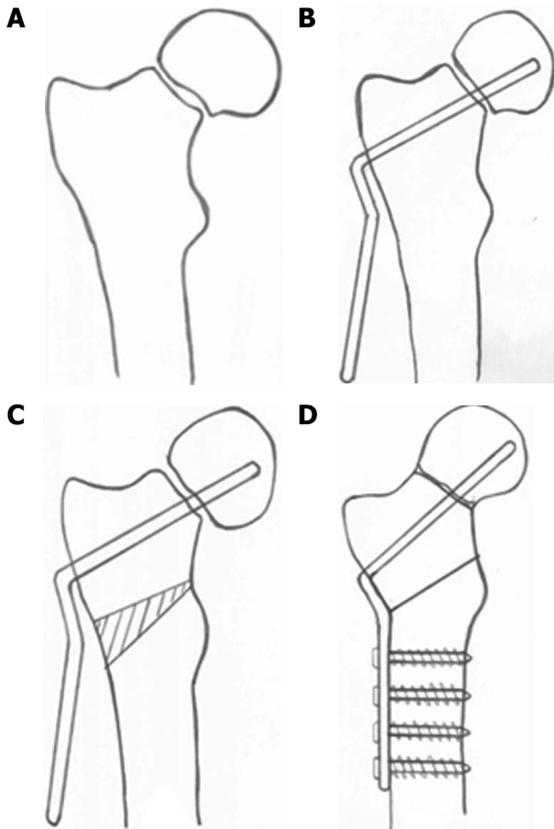


Figure 1 Diagram showing stages of valgus osteotomy. A: Closed reduction; B: Insertion of blade plate device; C: Excision of lateral wedge; D: Final correction after plate fixation.

of such a large wedge will cause the osteotomy to inevitably extend from the intertrochanteric region into the subtrochanteric, which may cause further distortion of the femoral anatomy and abduction as well as external rotation deformity^[16]. In addition, valgus of > 30 degrees can compromise the blood supply and increase the risk of AVN^[17]. Excessive valgus could also make a salvage total hip replacement extremely difficult.

Severely osteoporotic and short head fragments

These features complicate application of the fixation device, as they may not provide enough hold. Cases with these features should be treated with a replacement rather than a fixative device.

Too long or too short a blade length in a blade plate device

A too long blade length may hold the fracture site in distraction, while a too short blade length may not provide adequate hold in the proximal fragment. The 110 degree and 120 degree AO double angled blade plate is available at lengths of 65, 75 and 85 mm sizes. These lengths are sufficient for most patients. However it is our practice to keep an additional set of blade plates by cutting the blades in a lathe so that blade lengths of 55 mm upwards are available in 5 mm increments. This would take care of the occasional case where it maybe

required. The correct blade length cannot be over emphasized as in our opinion the impaction obtained is the single most factor to achieve union.

Position of blade plate in the femoral head

Previous fixation devices can create bone defects in the femoral head. Position of the blade plate in the head should be therefore in the strongest portion of the bone. Care should be taken to be not too superior or anterior, in the femoral head as this can lead to a potential cutout.

CONTROVERSIES

Valgus osteotomies and total hip arthroplasty

The advantages of valgus osteotomy are manifold and include preserving bone stock and avoiding total hip arthroplasty (THA) in young patients. THA in young patients is associated with higher complication rates, such as prosthesis loosening and infection, as well as higher revision rates^[18]. Though recent studies have shown increased survival rates in the young^[19], head salvage remains the preferable treatment, especially in a patient population which routinely sits cross-legged or squats. Therefore, while THA is the option of choice in patients who are physiologically older, head salvage *via* a valgus osteotomy is preferred for the younger patient population (Figure 2).

When performing an uncemented hip arthroplasty for a failed valgus osteotomy, care should be taken with the entry point so as to avoid reaming a false passage. While broaching care should be taken to negotiate over the tracts cut by the previous implants where a bridge of bone tends to form. An uncemented stem should have a distal fit and extend distal to the previous screw holes. The trochanteric fragment may remain as a nonunion and may have to be separately reattached to the femur. If the proximal femoral anatomy is grossly altered, due to a subtrochanteric osteotomy, a corrective osteotomy may be required. When there is a defect of the posteromedial cortex, use of special modular or calcar replacing stems may be required^[20].

If cemented arthroplasty is performed instead, care should be taken during cementation to pressurise the screw holes externally, as the cement can track out and cause devascularisation of the sandwiched bone. It is important to note that cemented THA has been shown to be successful in revising a failed valgus osteotomy. However they have been shown to have increased complication rates in terms of survival and infection rates as compared to primary total hip replacements^[21,22].

AVN and valgus osteotomy

Though the presence of radiological AVN preoperatively is not a contraindication for head salvage, the reported post-valgus osteotomy AVN rates range from 10% to 40%^[10,14,23]. Not all patients who develop AVN are symptomatic, and conversion rates to THA for treating

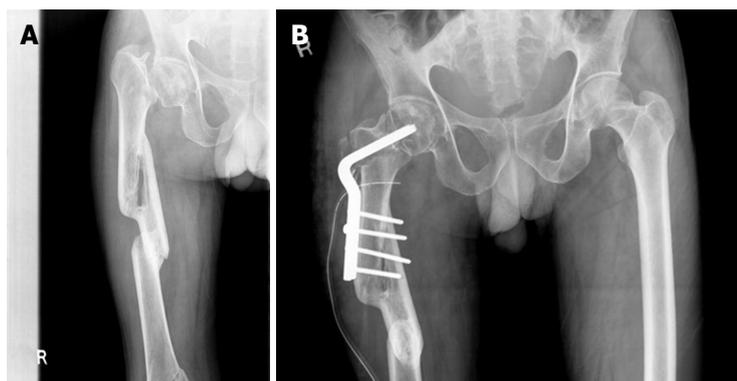


Figure 2 Problems with neglected fractures. A: Anteroposterior radiograph of pelvis of a 41-year-old male with a 3-mo-old nonunion neck of femur fracture and associated malunited femur fracture; B: At 4-year follow-up showing union, when the Harris hip score was 88.

post-valgus osteotomy AVN range from 5% to 10%^[10,14]. For patients with the aim of hip salvage, assessing the vascularity of the head may only be of academic value. However, a report of a small series of patients with nonunion and documented AVN who underwent valgus osteotomy with vascularized fibular graft demonstrated that arrest of AVN was achieved in 3 out of the 5 patients^[24].

Femoral neck shortening

Femoral neck shortening has been reported as associated with a poorer functional outcome in cases of acute NOF fractures^[25]. As most nonunion NOF have resorbed necks, this may be a predictive factor for outcome; however, no such correlation has been shown in a series reported recently^[14]. The intrinsic problem of nonunion femoral neck is the shortened neck fragment and, therefore, other options of head salvage, which can reconstruct the femoral neck length, may be effective^[8,26].

Choice of implant

The 110 and 120 degree angled blade plate, the 95 degree angled blade plate, a bent 95 degree blade plate, the sliding hip screw device, and a modified prebent dynamic condylar screw device have all been used as fixation devices for this surgery^[13,27-29]. However, surgeon's preference of implant remains largely subjective, as very little to no evidence from comparative, systematic analyses has been reported in the literature. Thus, the choice of implant may be based on the surgeon's familiarity, as long as the principles of implantation are adhered to.

PROGNOSTIC FACTORS AFFECTING OUTCOME

Evolution of philosophy

Most studies reporting valgus osteotomy emphasize union rates (Table 1) but are hampered by a lack of long-term follow-up and less than optimal functional outcome. Valgus intertrochanteric osteotomy primarily

aims to convert shear forces. Earlier studies attempted to convert a Pauwels 3 to a Pauwels 1 and attained union but with excessive valgus.

Marti *et al.*^[10] and Raaymakers *et al.*^[27] have shown that excessive valgus is detrimental to function (Figure 3). A more recent study showed that > 15 degrees of excess valgus, compared to the normal hip, results in poorer functional outcome^[14]. Thus, the philosophy has evolved over the years to promoting the reproduction of as normal a proximal femoral anatomy as possible (Figure 4). Imaging and radiographic analyses are complicated in cases presenting neck resorption; the recently-described head shaft angle measurement could be a useful tool for analyzing postoperative radiographs and prognosticating functional outcome.

It would be preferable to have clear indications and contraindications for attempting head salvage in patients with femoral neck nonunion. When considering union treatment, the size of the proximal fragment seems to be an important factor. However, measurement of the proximal fragment is a complicated issue. Sandhu *et al.*^[30] reported a study in which the patients were graded according to sizes of the proximal fragment and fracture gap; it was found that patients with a head size of < 2.5 cm had the worst outcome. This classification system has its own drawbacks^[11]. Magu *et al.*^[31] showed that the absolute head volume size of 43 mm³ or less, as measured by computed tomography scan, is associated with higher failure rates; however, the average volume of females in that series was 40.8 mm³, emphasizing the need for further studies in this area.

As femoral head size varies with patient height, sex and ethnicity, a ratio may be a better index than absolute size. Hence, a simple radiographic measurement called the neck resorption ratio (NRR) may be useful^[14]. The NRR is a measure of the remnant of the femoral head to the neck length on the sound side, and thus does not vary with traction or magnification of the plate X-ray and can be read on a simple anteroposterior pelvis radiograph. The three nonunion cases, which occurred in this study, were included in the group with an NRR of < 0.5. Thus, head salvage would be indicated in a physiologically young, active patient with sufficient bone

Table 1 Case series of valgus osteotomy for nonunion

Ref.	n	Average follow-up (yr)	Union rate, n/total (%)	AVN, n/total (%)	Implant	Functional outcome
Marti <i>et al</i> ^[10]	50	7.1	43/50 (86)	22/50 (44)	DABP	HHS: 91
Anglen <i>et al</i> ^[15]	13	2	13/13 (100)	2/13 (15)	DABP	HHS: 93
Wu <i>et al</i> ^[33]	32		32/32 (100)	2/32 (6)	SHS +/- (subtrochanteric osteotomy)	NA
Kalra <i>et al</i> ^[23] (neglected fractures)	22	2.5	20/22 (85)	2/22 (9)	DABP	75%; excellent to good results
Sringari <i>et al</i> ^[34]	20	2	18/20 (90)	Nil	DABP	NA
Magu <i>et al</i> ^[11]	48	6	44/48 (94)	2/48 (4)	DABP	HHS: 86.7
Khan <i>et al</i> ^[35]	16	2.5	14/16 (87)	Nil	SHS (120 degree plate)	HHS: 88
Said <i>et al</i> ^[29]	36	3.5	35/36 (97)	5/36 (13)	Angled blade plate (prebent 130 degree)	NA
Sen <i>et al</i> ^[26]	22	3.2	21/22 (91)	5/55 (22)	DABP + non-vasc fibula	66%; excellent to good results
Gadegone <i>et al</i> ^[7]	41	2.75	39/41 (95)	7/41 (17)	SHS (110-130 prebent plate + non-vasc fibula)	HHS: 90.9
Gavaskar <i>et al</i> ^[28]	11	1	11/11 (100)	Nil	SHS + subtrochanteric osteotomy, no wedge taken	Oxford score: 40
Gupta <i>et al</i> ^[36]	60	3.5	56/60 (93)	4/60 (6)	SHS (135 degree subtrochanteric osteotomy)	HHS: 87.5
Varghese <i>et al</i> ^[14]	32	5	29/32 (91)	13/32 (44)	DABP	HHS: 82

DABP: Double-angled blade plate; HHS: Harris hip score; NA: Not available; SHS: Sliding hip screw.

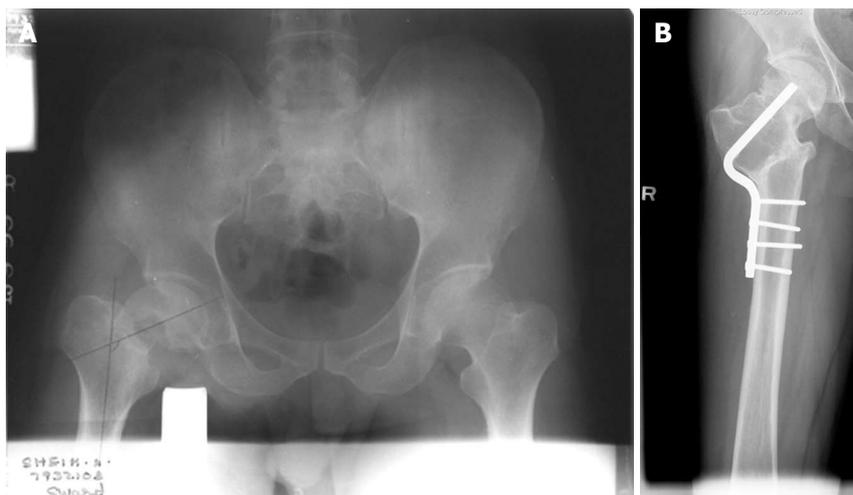


Figure 3 Problems with excess valgus. A: Anteroposterior radiograph of pelvis of a 33-year-old male with a 3-mo-old nonunion neck of femur fracture; B: At 10-year follow-up, showing excess valgus, when the Harris hip score was 68.

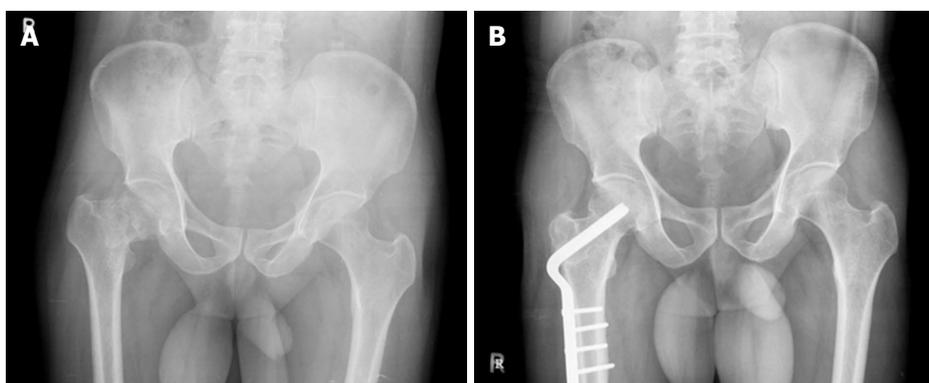


Figure 4 Ideal valgus correction. A: Anteroposterior radiograph of pelvis of a 45-year-old male with a 1-mo-old nonunion neck of femur fracture; B: At 5-year follow-up showing similar valgus orientation as the opposite hip, when the Harris hip score was 85.

stock and would be contraindicated in an older patient with an NRR of < 0.5.

CONCLUSION

There is a significant percentage of nonunion NOF in the young. Moreover in developing countries there is an additional problem of neglected fractures^[32]. It would appear that nonunions are increasingly being treated with arthroplasty, even in the young, with an additional need for revision. In this group of patients the valgus osteotomy would remain a viable alternative, especially in places where social and religious activities require squatting and sitting cross legged. Valgus osteotomy remains a successful method of head salvage in cases of nonunion and neglected NOF fractures. Excessive valgus may impair the final functional outcome; in cases presenting with resorbed neck (> 50%), arthroplasty would be a better option.

REFERENCES

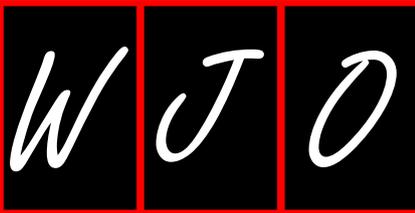
- 1 **Mathews V**, Cabanela ME. Femoral neck nonunion treatment. *Clin Orthop Relat Res* 2004; **(419)**: 57-64 [PMID: 15021132 DOI: 10.1097/00003086-200402000-00010]
- 2 **Lu-Yao GL**, Keller RB, Littenberg B, Wennberg JE. Outcomes after displaced fractures of the femoral neck. A meta-analysis of one hundred and six published reports. *J Bone Joint Surg Am* 1994; **76**: 15-25 [PMID: 8288658]
- 3 **Damany DS**, Parker MJ, Chojnowski A. Complications after intracapsular hip fractures in young adults. A meta-analysis of 18 published studies involving 564 fractures. *Injury* 2005; **36**: 131-141 [PMID: 15589931 DOI: 10.1016/j.injury.2004.05.023]
- 4 **Parker MJ**. Prediction of fracture union after internal fixation of intracapsular femoral neck fractures. *Injury* 1994; **25** Suppl 2: B3-B6 [PMID: 7960079 DOI: 10.1016/0020-1383(94)90229-1]
- 5 **Haidukewych GJ**, Berry DJ. Salvage of failed treatment of hip fractures. *J Am Acad Orthop Surg* 2005; **13**: 101-109 [PMID: 15850367 DOI: 10.5435/00124635-200503000-00003]
- 6 **Pauwels F**. Biomechanics of the normal and diseased hip. Springer Science and Business Media, 1976 [DOI: 10.1007/978-3-642-66212-6]
- 7 **Gadegone WM**, Ramteke AA, Lokhande V, Salphade Y. Valgus intertrochanteric osteotomy and fibular strut graft in the management of neglected femoral neck fracture. *Injury* 2013; **44**: 763-768 [PMID: 23063702 DOI: 10.1016/j.injury.2012.09.014]
- 8 **LeCroy CM**, Rizzo M, Gunneson EE, Urbaniak JR. Free vascularized fibular bone grafting in the management of femoral neck nonunion in patients younger than fifty years. *J Orthop Trauma* 2002; **16**: 464-472 [PMID: 12172276 DOI: 10.1097/00005131-200208000-00004]
- 9 **Meyers MH**, Harvey JP, Moore TM. Delayed treatment of subcapital and transcervical fractures of the neck of the femur with internal fixation and a muscle pedicle bone graft. *Orthop Clin North Am* 1974; **5**: 743-756 [PMID: 4606412]
- 10 **Marti RK**, Schüller HM, Raaymakers EL. Intertrochanteric osteotomy for non-union of the femoral neck. *J Bone Joint Surg Br* 1989; **71**: 782-787 [PMID: 2584247]
- 11 **Magu NK**, Rohilla R, Singh R, Tater R. Modified Pauwels' intertrochanteric osteotomy in neglected femoral neck fracture. *Clin Orthop Relat Res* 2009; **467**: 1064-1073 [PMID: 19142687 DOI: 10.1007/s11999-008-0695-4]
- 12 **Muller ME**. Intertrochanteric osteotomy: indications, preoperative planning, technique. Berlin: Springer-Verlag, 1984: 25-66 [DOI: 10.1007/978-3-642-68052-6_3]
- 13 **Deakin DE**, Guy P, O'Brien PJ, Blachut PA, Lefavre KA. Managing failed fixation: valgus osteotomy for femoral neck nonunion. *Injury* 2015; **46**: 492-496 [PMID: 25530407 DOI: 10.1016/j.injury.2014.11.022]
- 14 **Varghese VD**, Boopalan PR, Titus VT, Oommen AT, Jepeganiam TS. Indices affecting outcome of neglected femoral neck fractures after valgus intertrochanteric osteotomy. *J Orthop Trauma* 2014; **28**: 410-416 [PMID: 24164787 DOI: 10.1097/BOT.0000000000000030]
- 15 **Anglen JO**. Intertrochanteric osteotomy for failed internal fixation of femoral neck fracture. *Clin Orthop Relat Res* 1997; **(341)**: 175-182 [PMID: 9269172 DOI: 10.1097/00003086-199708000-00027]
- 16 **Magu NK**, Singh R, Mittal R, Garg R, Wokhlu A, Sharma AK. Osteosynthesis and primary valgus intertrochanteric osteotomy in displaced intracapsular fracture neck of femur with osteoporosis in adults. *Injury* 2005; **36**: 110-122 [PMID: 15589929 DOI: 10.1016/j.injury.2004.02.017]
- 17 **Calandruccio RA**, Anderson WE. Post-fracture avascular necrosis of the femoral head: correlation of experimental and clinical studies. *Clin Orthop Relat Res* 1980; **(152)**: 49-84 [PMID: 7438624]
- 18 **Gililand JM**, Anderson LA, Erickson J, Pelt CE, Peters CL. Mean 5-year clinical and radiographic outcomes of cementless total hip arthroplasty in patients under the age of 30. *Biomed Res Int* 2013; **2013**: 649506 [PMID: 23865060 DOI: 10.1155/2013/649506]
- 19 **Wroblewski BM**, Siney PD, Fleming PA. Charnley low-frictional torque arthroplasty: follow-up for 30 to 40 years. *J Bone Joint Surg Br* 2009; **91**: 447-450 [PMID: 19336802 DOI: 10.1302/0301-620X.91B4.21933]
- 20 **Haidukewych GJ**, Berry DJ. Hip arthroplasty for salvage of failed treatment of intertrochanteric hip fractures. *J Bone Joint Surg Am* 2003; **85-A**: 899-904 [PMID: 12728042]
- 21 **Ferguson GM**, Cabanela ME, Ilstrup DM. Total hip arthroplasty after failed intertrochanteric osteotomy. *J Bone Joint Surg Br* 1994; **76**: 252-257 [PMID: 8113286]
- 22 **Breusch SJ**, Lukoschek M, Thomsen M, Mau H, Ewerbeck V, Aldinger PR. Ten-year results of uncemented hip stems for failed intertrochanteric osteotomy. *Arch Orthop Trauma Surg* 2005; **125**: 304-309 [PMID: 15742190 DOI: 10.1007/s00402-005-0800-z]
- 23 **Kalra M**, Anand S. Valgus intertrochanteric osteotomy for neglected femoral neck fractures in young adults. *Int Orthop* 2001; **25**: 363-366 [PMID: 11820442]
- 24 **Beris AE**, Payatakes AH, Kostopoulos VK, Korompilias AV, Mavrodontidis AN, Vekris MD, Kontogeorgakos VA, Soucacos PN. Non-union of femoral neck fractures with osteonecrosis of the femoral head: treatment with combined free vascularized fibular grafting and subtrochanteric valgus osteotomy. *Orthop Clin North Am* 2004; **35**: 335-343, ix [PMID: 15271541 DOI: 10.1016/j.ocl.2004.02.008]
- 25 **Zlowodzki M**, Ayeni O, Petrisor BA, Bhandari M. Femoral neck shortening after fracture fixation with multiple cancellous screws: incidence and effect on function. *J Trauma* 2008; **64**: 163-169 [PMID: 18188116 DOI: 10.1097/01.ta.0000241143.71274.63]
- 26 **Sen RK**, Tripathy SK, Goyal T, Aggarwal S, Tahasildar N, Singh D, Singh AK. Osteosynthesis of femoral-neck nonunion with angle blade plate and autogenous fibular graft. *Int Orthop* 2012; **36**: 827-832 [PMID: 21881882 DOI: 10.1007/s00264-011-1344-1]
- 27 **Raaymakers EL**, Marti RK. Nonunion of the femoral neck: possibilities and limitations of the various treatment modalities. *Indian J Orthop* 2008; **42**: 13-21 [PMID: 19823649 DOI: 10.4103/0019-5413.38575]
- 28 **Gavaskar AS**, Chowdary NT. Valgus sliding subtrochanteric osteotomy for neglected fractures of the proximal femur; surgical technique and a retrospective case series. *J Orthop Surg Res* 2013; **8**: 4 [PMID: 23497534 DOI: 10.1186/1749-799X-8-4]
- 29 **Said GZ**, Farouk O, Said HG. Valgus intertrochanteric osteotomy with single-angled 130° plate fixation for fractures and non-unions of the femoral neck. *Int Orthop* 2010; **34**: 1291-1295 [PMID: 19946774 DOI: 10.1007/s00264-009-0885-z]
- 30 **Sandhu HS**, Sandhu PS, Kapoor A. Neglected fractured neck of the femur: a predictive classification and treatment by osteo-

- synthesis. *Clin Orthop Relat Res* 2005; **(431)**: 14-20 [PMID: 15685050]
- 31 **Magu NK**, Magu S, Rohilla RK, Batra A, Jaipuria A, Singh A. Computed tomographic evaluation of the proximal femur: A predictive classification in displaced femoral neck fracture management. *Indian J Orthop* 2014; **48**: 476-483 [PMID: 25298554 DOI: 10.4103/0019-5413.139857]
- 32 **Jain AK**, Mukunth R, Srivastava A. Treatment of neglected femoral neck fracture. *Indian J Orthop* 2015; **49**: 17-27 [PMID: 25593354 DOI: 10.4103/0019-5413.143909]
- 33 **Wu CC**, Shih CH, Chen WJ, Tai CL. Treatment of femoral neck nonunions with a sliding compression screw: comparison with and without subtrochanteric valgus osteotomy. *J Trauma* 1999; **46**: 312-317 [PMID: 10029039]
- 34 **Sringari T**, Jain UK, Sharma VD. Role of valgus osteotomy and fixation by double-angle blade plate in neglected displaced intracapsular fracture of neck of femur in younger patients. *Injury* 2005; **36**: 630-634 [PMID: 15826623]
- 35 **Khan AQ**, Khan MS, Sherwani MK, Agarwal R. Role of valgus osteotomy and fixation with dynamic hip screw and 120 degrees double angle barrel plate in the management of neglected and ununited femoral neck fracture in young patients. *J Orthop Traumatol* 2009; **10**: 71-78 [PMID: 19484358 DOI: 10.1007/s10195-009-0049-3]
- 36 **Gupta S**, Kukreja S, Singh V. Valgus osteotomy and repositioning and fixation with a dynamic hip screw and a 135° single-angled barrel plate for un-united and neglected femoral neck fractures. *J Orthop Surg (Hong Kong)* 2014; **22**: 13-17 [PMID: 24781606]

P- Reviewer: Aprato A, Carbone S **S- Editor:** Ji FF

L- Editor: A **E- Editor:** Liu SQ





Prospective Study

From Cape Town to Cambridge: Orthopaedic trauma in contrasting environments

John E Lawrence, Vikas Khanduja

John E Lawrence, Vikas Khanduja, Department of Trauma and Orthopaedics, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge CB2 0QQ, United Kingdom

Author contributions: Lawrence JE and Khanduja V contributed equally to this work; Lawrence JE gathered the data, performed data analysis and drafted the manuscript; Khanduja V devised the study, assisted with data analysis and edited the manuscript.

Institutional review board statement: This study was approved by both Addenbrooke's Hospital, Cambridge and New Somerset Hospital, Cape Town.

Informed consent statement: All patients gave verbal informed consent for their anonymised data to be used in this study.

Conflict-of-interest statement: The authors of this manuscript having no conflicts of interest to disclose.

Data sharing statement: Extended dataset available from the corresponding author at vk279@cam.ac.uk.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Vikas Khanduja, MA, MSc, FRCS, FRCS (Orth), Consultant Orthopaedic Surgeon, Department of Trauma and Orthopaedics, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Box 37, Hills Road, Cambridge CB2 0QQ, United Kingdom. vk279@cam.ac.uk
Telephone: +44-1223-257093

Received: November 24, 2015
Peer-review started: November 25, 2015
First decision: December 28, 2015

Revised: January 6, 2016
Accepted: March 7, 2016
Article in press: March 9, 2016
Published online: May 18, 2016

Abstract

AIM: To compare the trauma experience gained by a trainee at a United Kingdom major trauma centre and a secondary level hospital in South Africa.

METHODS: A profile of inpatient trauma cases during a five-week period in Addenbrooke's Hospital, Cambridge and Somerset Hospital, Cape Town was created. This was achieved by recording various parameters for each patient admitted including age, gender, injury, mechanism of injury and postal/area code. This, together with details of the departments themselves, allows a comparison of the amount and variety of orthopaedic trauma cases experienced by an individual trainee in each setting.

RESULTS: The trauma profiles differed significantly. Patients in Cape Town were younger and more likely to be male. In the young, injury in Cape Town was more likely to occur due to assault or being struck by a vehicle, whilst patients in Cambridge were more likely to be injured whilst in a vehicle or in high energy falls. In older patients, trauma at both centres was almost exclusively due to mechanical falls. In a given age group, injuries at the two centres were similar, however the majority of patients admitted to Addenbrooke's were elderly, resulting in less variation in the overall injury profile.

CONCLUSION: The trauma profile of a major trauma centre in the United Kingdom is less varied than that of a South African secondary centre, with significantly fewer cases per surgeon. This suggests a more varied

training experience in the developing world with a greater caseload.

Key words: Comparative; Epidemiology; Developing world; Trauma; Training

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The caseload of a hospital directly impacts the training experience of a surgeon. Centres in the developing world are widely thought to offer a superior exposure to traumatic injury and consequently a rich training environment for the orthopaedic trainee. This study directly compares the caseload at two centres over a fixed period, and shows that the department in the developing world experienced greater volume and variation in trauma cases thereby offering a better experience for training in trauma.

Lawrence JE, Khanduja V. From Cape Town to Cambridge: Orthopaedic trauma in contrasting environments. *World J Orthop* 2016; 7(5): 308-314 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/308.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.308>

INTRODUCTION

Injury secondary to trauma is a major public health issue. It is a leading cause of death world wide, with road traffic accidents alone accounting for 1.2 million deaths per year^[1]. By 2020, musculoskeletal injury will account for 20% of all the world's disability-adjusted life years. The vast majority of this burden lies with the developing world with low and middle-income countries entering the third phase of epidemiologic transition. This entails an increase in the average life expectancy and a consequent exposure of the population to the so-called man-made diseases^[2-4]. Despite this growing burden, orthopaedic care in the developing world remains scarce when compared with developed countries, with only one in three people provided for^[5].

This disparity in demand and supply of orthopaedic care has implications for orthopaedic training across the globe. This study profiled the orthopaedic trauma admissions at two centres in contrasting settings; one a major trauma centre in Cambridge, United Kingdom, the other a secondary level centre in Cape Town, South Africa. These two counties exemplify the difference in disease burden, with injury accounting for 2.7% and 9% of deaths respectively^[6,7]. A comparison would therefore make it possible to quantify how this increased burden in the developing world influences the experience of the orthopaedic trainee in South Africa in comparison with the trainee in the United Kingdom.

The aim of the study, therefore, was to compare, contrast and objectively quantify the trauma admissions

that a trainee would be exposed to whilst based in Cambridge, United Kingdom and in Cape Town, South Africa. This in turn would have implications for those intending to train in trauma surgery.

MATERIALS AND METHODS

Study hospitals

New Somerset Hospital is a secondary level state hospital situated in Green Point, a district in the north-west of Cape Town. It serves the central health district of the city, which holds a population of 800000. The orthopaedic department is staffed by one full-time Consultant, one part-time consultant and two medical officers (equivalent to the core surgical trainee in the United Kingdom). Two internship doctors (equivalent to foundation programme year one doctors) staff the ward, which consists of twenty-three beds; three bays of six patients and one bay of five patients. Each bay is staffed by a staff nurse, with a ward sister overseeing care on the ward. The department admits all patients aged 13 or over, with paediatric cases referred to the regional paediatric hospital.

By contrast, Addenbrooke's Hospital is the major trauma centre for the East of England, providing tertiary trauma care to a population of 5.4 million. It has seventy-two orthopaedic beds and is staffed by sixteen Consultants, ten specialist registrars and eight senior house officers (a mix of foundation year two doctors, core surgical trainees and junior clinical fellows). The wards consist of several bays and side rooms with one trained nurse for every five patients and senior and junior sisters for each ward. In addition, the department is staffed by a team of three trauma specialist nurses who co-ordinate admissions and administer specialist nursing care on the wards. The Department has a recently expanded and now houses an Orthopaedic Trauma Unit that is run by 5 Consultants specialising in Trauma and essentially manages all the multiply injured patients admitted to the Hospital. The unit admits patients of all ages.

The period of the study at New Somerset Hospital ran during from June to July 2012, and the study at Addenbrooke's Hospital in Cambridge ran from August to September 2012.

Data collection

This was a prospective study that included all the orthopaedic trauma admissions during a five-week period at each hospital. For each admitted patient, a multitude of parameters were recorded in order to form an overall profile of the orthopaedic trauma. These were age, sex, injury by anatomical site, mechanism of injury [mechanical fall, high energy fall, sporting, interpersonal, pedestrian motor vehicle accident and in - car motor vehicle accident (cMVA)] and postal/area code.

Statistical analysis

Statistical analysis was carried out using SPSS Version

Table 1 The numbers of the more common injuries at each centre

Injury site	Mean patient age - Cambridge (n)	Mean patient age - Cape Town (n)
Proximal radius and ulna	45.8 (6)	35.6 (5)
Distal radius and ulna	25.3 (12)	42.3 (4)
Intracapsular neck of femur	81.9 (16)	74.5 (6)
Extracapsular neck of femur	80.8 (27)	78.2 (5)
Proximal tibia	47.5 (4)	26.4 (5)
Tibial/fibular diaphysis	37.1 (7)	42.1 (8)
Tibia/fibula	44.8 (12)	49.8 (7)

Table 2 The frequency of each mechanism of injury at each centre

Mechanism	Patients - Cambridge (%)	Mean age (yr) - Cambridge	Patients - Cape Town (%)	Mean age (yr) - Cape Town
Mechanical fall	76 (52.8)	71.5	30 (47.6)	57.7
High energy fall	31 (21.5)	36.9	5 (7.9)	28.2
cMVA	16 (11.1)	45.4	4 (6.3)	41.5
pMVA	6 (4.2)	39.2	6 (9.5)	39.3
Interpersonal	1 (0.7)	68	10 (15.9)	34
Sporting	15 (10.4)	22.2	8 (12.7)	26.8

pMVA: Pedestrian motor vehicle accident; cMVA: Car motor vehicle accident.

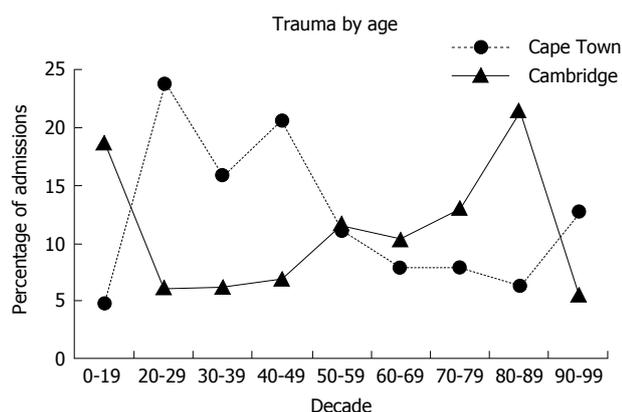


Figure 1 A graph showing age of patients admitted to both centres.

13 for all the variables.

RESULTS

Trauma by age and gender

There were 63 orthopaedic trauma admissions to the New Somerset Hospital during the study period; 40 males and 23 females with a mean age of 44.9 years. The youngest patient admitted was 14 and the oldest 96. The highest rate of admissions was observed in the 20-29 years age group.

Addenbrooke's Hospital admitted 144 patients during the study period with equal numbers of male and female patients and a mean age of 54.8 years (range 1 to 97 years), with the highest admission rate in the 80-89 age group. Of these patients, 125 were aged 13 or older, and the average age in this group was 62.4 years. The age distribution of trauma at the two centres is shown in Figure 1.

Trauma by injury and mechanism

Injury was categorised by anatomical region using the AO fracture classification. At New Somerset, tibial fractures were the most common ($n = 22$, 34.9%), particularly those involving the diaphysis and malleoli, followed by fractures of the proximal femur ($n = 11$, 17.5%) and fractures of the radius and ulna ($n = 10$, 15.9%).

At Addenbrooke's hospital, fractures of the proximal femur were the most common injury ($n = 50$, 34.7%), followed by fractures of the tibia ($n = 24$, 16.7%) and fractures of the radius and ulna ($n = 23$, 16%). The common fracture sites for both centres are compared in Figure 2. Table 1 shows the mean age for the common injury sites at both centres.

Mechanism of injury was divided into six categories. The frequency of each of these categories, together with the mean age for each mechanism, is summarised in Table 2.

Mechanical fall was the most common mechanism of injury for both centres, accounting for 52.8% of injuries at Addenbrooke's and 47.6% of injuries at New Somerset. High-energy falls were the second most common mechanism at Addenbrooke's (21.5%), followed by in - cMVAs (11.1%). Interpersonal mechanisms were the second most common at New Somerset (15.9%), followed by sporting incidents (12.7%). Mechanisms of injury in the under-45 and 45 and over age groups at both centres are shown in Figure 3. Mechanical falls (25.7%) and interpersonal actions (22.9%) were the most common cause of injury in the under-45 s in Cape Town, with high-energy falls (40%) and in - cMVAs (26.7%) the most common in this age group in Cambridge.

In the over-45 age group, mechanical falls were the

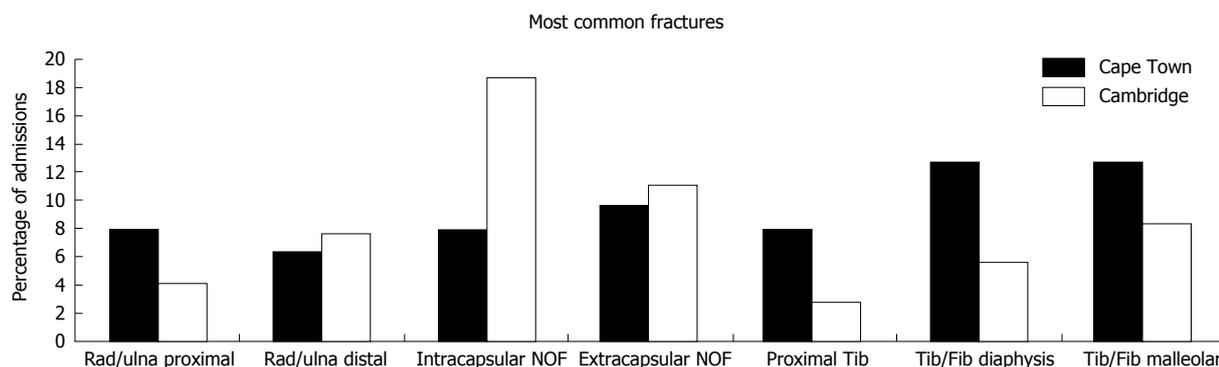


Figure 2 A bar chart showing the most common fracture sites at each centre by anatomical distribution. Rad: Radius; Tib: Tibia; Fib: Fibula; NOF: Neck of femur.

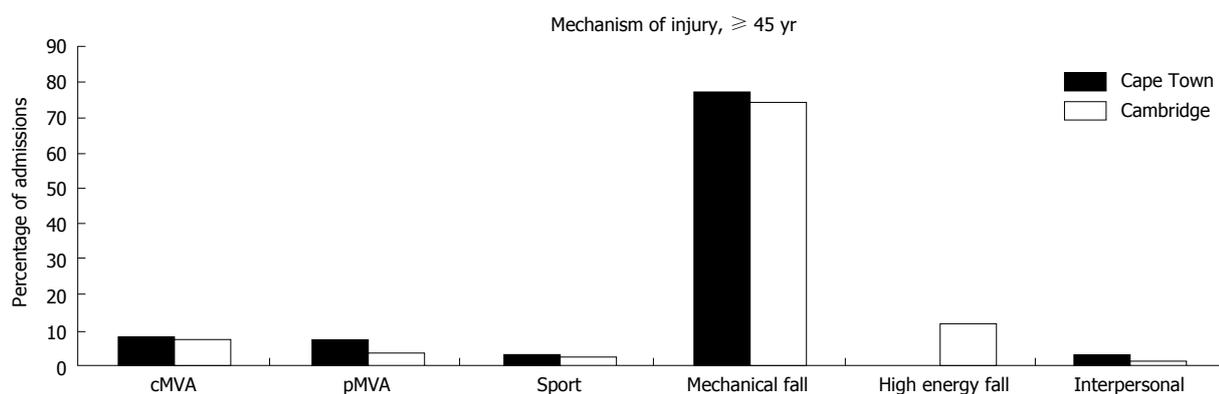


Figure 3 A bar chart showing mechanism of injury in patients aged 45 and over. pMVA: Pedestrian motor vehicle accident; cMVA: Car motor vehicle accident.

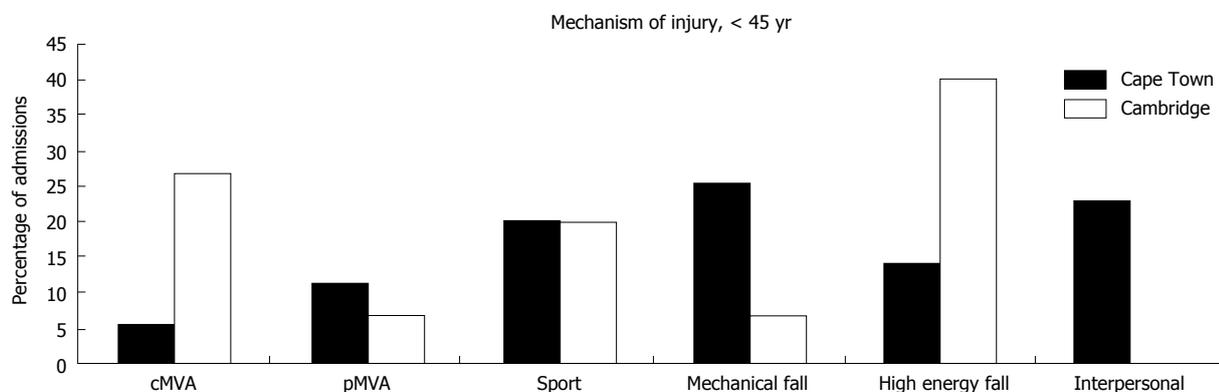


Figure 4 A bar chart showing mechanism of injury in patients aged under 45. pMVA: Pedestrian motor vehicle accident; cMVA: Car motor vehicle accident.

main mechanism, accounting for 74.5% and 77.8% of injuries in Cambridge and Cape Town respectively. These trends are summarized in Figure 3.

Trauma by location

Location was recorded at each admission using patient postal code. At New Somerset, the mean distance from patient address to hospital was 21.1 miles, with the median distance 11 miles. Distances ranged from 1 mile to 93 miles. The mean distance between patient address and Addenbrooke’s hospital was 18.6 miles and the median distance was 13.5 miles. Distances ranged from 2 miles to 98 miles.

Geographical distribution of trauma cases is summarized in Figure 4. The distances at Addenbrooke’s Hospital were more normally distributed, whereas the distances at New Somerset Hospital were more positively skewed with a second group of admissions corresponding to outreach services provided by the hospital.

DISCUSSION

The trauma profile at Addenbrooke’s hospital, Cambridge was markedly different to that of New Somerset Hospital, Cape Town. Patients at New Somerset were younger and more likely to be male. In both centres,

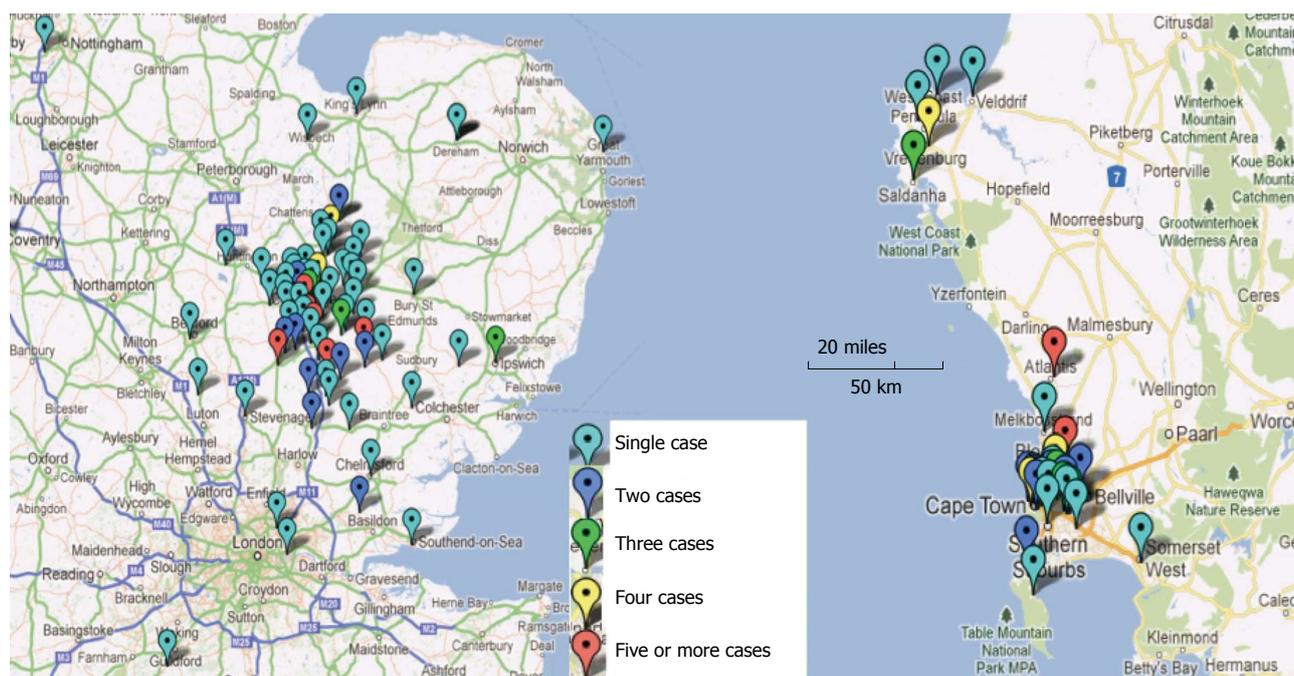


Figure 5 A composite map, to scale, showing the geographical location of trauma in Cambridge (left) and Cape Town (right).

there was a similar injury pattern in any given age group, with a notably broader range of injury in younger patients. However, the patients admitted to New Somerset Hospital were of lower average age, resulting in a much more varied overall injury profile at this centre.

Patients in the younger age groups admitted to New Somerset Hospital were more likely to be injured by interpersonal means or following pedestrian motor vehicle accidents than patients in the same age group admitted to Addenbrooke’s Hospital, who were more likely to be injured following an in - cMVA or a high energy fall. These differences reflect the hospitals and their settings; Addenbrooke’s Hospital is a level one trauma centre and is therefore specifically tasked with treating more high energy trauma injuries such as those sustained during in-car motor vehicle accidents or high energy falls. Conversely, new Somerset Hospital serves an area with high rates of interpersonal crime, leading to more injuries sustained by these mechanisms. In the elderly, trauma at both centres was almost exclusively due to mechanical falls with the majority of injuries being fragility fractures.

The geographical distribution of cases at the two centres was comparable, with a similar average distance and range of distances between patient address and hospital. The distances between patient address and Addenbrooke’s Hospital were more normally distributed than those at New Somerset Hospital. This is in keeping with the role of Addenbrooke’s Hospital as a major trauma centre, taking referrals from all parts of the East of England. The distribution of distances between patient address and New Somerset Hospital showed a clear bimodal distribution. These two groups reflect

the two distinct areas served by the hospital; the first being western and central Cape Town and the second corresponding to patients admitted from outreach clinics in rural communities far from the hospital (Figure 5).

In order to fully analyse the experience of a trainee, these trauma profiles must be placed in the context of the two centres. Although Addenbrooke’s Hospital admitted more than twice the number of patients than New Somerset Hospital, it employs a significantly larger workforce, with a total of thirty-four surgeons (eighteen trainees, sixteen consultants) to New Somerset’s four (two trainees, one full-time consultant and one part-time consultant). This imbalance in the number of surgeons results in a much greater trauma caseload for the trainee in Cape Town, South Africa. This, together with the more varied injury profile at New Somerset Hospital, enables the trainee to gain wider experience in the management of orthopaedic trauma.

Whilst caseload is an important aspect of surgical training, it is not the sole determinant of its quality. The training programmes in both countries follow the traditional apprenticeship model and are largely comparable, with some subtle differences which should be understood when comparing the experience gained by a trainee. In South Africa, orthopaedic training is undertaken following a two year internship and community service year. Training takes place at one of nine accredited universities, two of which are accredited for the first two years of the training programme only. This is similar to the structure of training in the United Kingdom which takes place in one of twelve regions in England, Wales and Northern Ireland (Scotland has a separate training structure). Each region contains at least one teaching hospital linked to a university. United

Kingdom medical graduates undertake a two-year foundation training programme analogous to that of the South African internship, however there is no equivalent to the community service year in the United Kingdom. Instead, trainees must complete the two-year core surgical training programme before applying for specialty training in orthopaedics.

Both South African and United Kingdom orthopaedic specialty training programmes typically last for five years, and require the completion of various examinations in order to progress. In South Africa, training works on the basis of three levels of study. The first level is assessed with the primary examination, which focuses on basic surgical sciences such as pathology and anatomy. The second level of study concludes with the orthopaedic intermediate examination, which focuses on the clinical aspects of surgery, with a focus on orthopaedics. Enrollment in the intermediate examination requires candidates to have eighteen months of experience in one of the aforementioned university hospitals, including intensive care and trauma experience. The final part of training involves six month rotations through the various orthopaedic sub-specialties with attachment to a consultant for each rotation. During this part of training, trainees must publish at least one research article. Upon completion of three years of rotations, trainees may register for the final examinations, the fellowship of the college of orthopaedic surgeons of South Africa, meaning a surgeon can be fully qualified eight years after graduation from medical school.

Orthopaedic specialty training in the United Kingdom follows a similar pattern, though trainees must attain Membership of the Royal College of Surgeons (MRCS) prior to the commencement of specialist training. This involves passing two examinations; the first a written exam with a focus on basic surgical sciences and principles of surgery in general and the second an objective structured clinical examination which focuses on applied surgical sciences with practical and communication skills. In this regard, the MRCS is comparable to a combination of the primary and intermediate examinations in South Africa, though it lacks specificity to orthopaedics. In a similar fashion to South Africa, the training programme lasts for five years and involves six month rotations through sub-specialties with attachment to a consultant. Like South Africa, trainees take the Fellowship of the Royal College of Surgeons after three or four years of specialty training. Trainees are expected to regularly partake in research and quality improvement. Overall, trainees can be expected to complete training nine to ten years post-graduation^[8,9].

Both training programmes have a set of competencies which are expected to be achieved at the completion of training. This essentially requires trainees to be competent in a range of orthopaedic procedures, with competency defined as the completion of a defined number of cases.

The apprenticeship nature of surgical training means

much depends on the quality of the mentor, meaning there will always be natural variation in the quality of training. However, the similarity of the training programmes in these two countries places emphasis on the quantity and type of orthopaedic trauma experienced by a trainee. This study shows trainees at Addenbrooke's Hospital experience fewer cases than their counterparts at New Somerset Hospital, and the cases they do experience are less varied.

To this end, the study highlights the potential benefits of establishing training programmes that combines the structure of a United Kingdom major trauma centre with the volume and variation provided by hospitals in the developing world. Currently, trainees in the United Kingdom are able to apply to their regional training body for out of programme clinical experience (OOPE), which can take the form of work in the developing world. Whilst studies such as ours highlight the potential benefits this would hold for the trainee, time out of programme does not often gain approval for clinical training and thus can delay career progression, making it an unpopular choice amongst trainees.

An alternative to OOPE is an approved fellowship abroad. Several studies have shown the benefits of establishing synergistic partnerships between hospitals in the developing and developed worlds, whereby trainees from each centre swap roles in order to broaden their surgical experience^[10,11]. We believe that expanding the number and variety of such fellowships will help surgeons worldwide to establish best practices and increase the standard of trauma care in a time when traumatic injury is increasing at an alarming rate.

COMMENTS

Background

Traumatic injury is rapidly increasing in the developing world as many countries enter the third phase of epidemiological transition. This has wide-ranging implications for surgical training, with trainees in the developing world thought to gain greater experience in the management of orthopaedic trauma. The study aimed to compare the experience gained in orthopaedic trauma at United Kingdom major trauma centre and a secondary level South African centre.

Research frontiers

Restrictions on working hours have placed additional strain on the training of surgeons, and this study suggests a potential mutual benefit lies in training periods spent in the developing world.

Innovations and breakthroughs

This is the first study to directly compare the orthopaedic trauma experience gained in South African and United Kingdom hospitals, showing a greater caseload with more variation in South Africa. The study adds to the literature on the utility of out of programme experience and exchange fellowships.

Applications

This study supports the expansion of both out of programme experience and exchange fellowships in trauma and orthopaedic training.

Terminology

Out of programme experience: Time spent by a United Kingdom trainee away from their training institution.

Peer-review

The authors have performed a good study, the manuscript is interesting.

REFERENCES

- 1 **World Health Organization.** World health report 2002. Statistical annex 3: burden of disease in DALYs by cause, sex and mortality stratum in WHO regions. 2001. Available from: URL: <http://www.who.int/whr/2002/annex/en/>
- 2 **Spiegel DA, Nduaguba A, Cherian MN, Monono M, Kelley ET.** Deficiencies in the availability of essential musculoskeletal surgical services at 883 health facilities in 24 low- and lower-middle-income countries. *World J Surg* 2015; **39**: 1421-1432 [PMID: 25663008 DOI: 10.1007/s00268-015-2971-2]
- 3 **Moroz PJ, Spiegel DA.** The World Health Organization’s action plan on the road traffic injury pandemic: is there any action for orthopaedic trauma surgeons? *J Orthop Trauma* 2014; **28** Suppl 1: S11-S14 [PMID: 24857989 DOI: 10.1097/BOT.0000000000000105]
- 4 **Murray CJL, Lopez AD.** Global Burden of Disease and Injury Series, vol II. The Harvard School of Public Health, 1996. Available from: URL: http://apps.who.int/iris/bitstream/10665/41864/1/0965546608_eng.pdf
- 5 **Brouillette MA, Kaiser SP, Konadu P, Kumah-Ametepey RA, Aidoo AJ, Coughlin RC.** Orthopedic surgery in the developing world: workforce and operative volumes in Ghana compared to those in the United States. *World J Surg* 2014; **38**: 849-857 [PMID: 24218152 DOI: 10.1007/s00268-013-2314-0]
- 6 **Bradshaw D, Pillay-Van Wyk V, Laubscher R, Nojilana B, Groenewald P, Nannan N, Metcalf C.** Cause of death statistics for South Africa: Challenges and possibilities for improvement. Cape Town, SA: Medical Research Council, 2012. Available from: URL: http://www.mrc.ac.za/bod/cause_death_statsSA.pdf
- 7 **Office for National Statistics.** Deaths Registered in England and Wales. 2010. Available from: URL: <http://www.ons.gov.uk/ons/rel/vsobl/mortality-statistics--deaths-registered-in-england-and-wales--series-dr-/2011/stb-deaths-registered-in-england-and-wales-in-2011-by-cause.html>
- 8 **The Royal College of Surgeons.** England Emergency Surgery: Standards for Unscheduled Care. 2011. Available from: URL: <http://www.rcseng.ac.uk/publications/docs/emergency-surgery-standards-for-unscheduled-care>
- 9 **Inaparthi PK, Sayana MK, Maffulli N.** Evolving trauma and orthopedics training in the UK. *J Surg Educ* 2013; **70**: 104-108 [PMID: 23337678 DOI: 10.1016/j.jsurg.2012.07.006]
- 10 **Hoehn RS, Davis BR, Huber NL, Edwards MJ, Lungu D, Logan JM.** A systematic approach to developing a global surgery elective. *J Surg Educ* 2015; **72**: e15-e20 [PMID: 25817013 DOI: 10.1016/j.jsurg.2015.01.011]
- 11 **Tyler WK, Mir HR, Zlotolow DA, Kroonen LT.** The AOA-JOA 2014 exchange traveling fellowship: Banzai and beyond. *J Bone Joint Surg Am* 2015; **97**: e22 [PMID: 25695993 DOI: 10.2106/JBJS.N.00873]

P- Reviewer: Anand A, Finestone AS, Luo XH **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Liu SQ



Management of lumbar zygapophysial (facet) joint pain

Laxmaiah Manchikanti, Joshua A Hirsch, Frank JE Falco, Mark V Boswell

Laxmaiah Manchikanti, Pain Management Center of Paducah, Paducah, KY 42003, United States

Laxmaiah Manchikanti, Mark V Boswell, Anesthesiology and Perioperative Medicine, University of Louisville, Louisville, KY 40292, United States

Joshua A Hirsch, NeuroInterventional Services and Neuroendovascular Program, Massachusetts General Hospital, Boston, MA 02114, United States

Joshua A Hirsch, Harvard Medical School, Boston, MA 02115, United States

Frank JE Falco, Mid Atlantic Spine and Pain Physicians, Newark, DE 19702, United States

Frank JE Falco, Pain Medicine Fellowship Program, Temple University Hospital, Philadelphia, PA 19140, United States

Author contributions: Manchikanti L, Hirsch JA, Falco FJE and Boswell MV contributed to this work; Manchikanti L and Boswell MV designed the research; Manchikanti L and Falco FJE performed the research; Manchikanti L and Hirsch JA contributed new reagents/analytic tools, analyzed the data and wrote the paper; all authors reviewed all contents and approved for submission.

Conflict-of-interest statement: No potential conflicts of interest relevant to this article were reported.

Data sharing statement: There is no such statement required. This manuscript has not described any basic research or clinical research.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Laxmaiah Manchikanti, MD, Medical Director of the Pain Management Center of Paducah, Clinical

Professor, Pain Management Center of Paducah, 2831 Lone Oak Road, Paducah, KY 42003, United States. drim@thepainmd.com
Telephone: +1-270-5548373-101
Fax: +1-270-5548987

Received: June 9, 2015

Peer-review started: June 11, 2015

First decision: September 30, 2015

Revised: January 14, 2016

Accepted: January 27, 2016

Article in press: January 29, 2016

Published online: May 18, 2016

Abstract

AIM: To investigate the diagnostic validity and therapeutic value of lumbar facet joint interventions in managing chronic low back pain.

METHODS: The review process applied systematic evidence-based assessment methodology of controlled trials of diagnostic validity and randomized controlled trials of therapeutic efficacy. Inclusion criteria encompassed all facet joint interventions performed in a controlled fashion. The pain relief of greater than 50% was the outcome measure for diagnostic accuracy assessment of the controlled studies with ability to perform previously painful movements, whereas, for randomized controlled therapeutic efficacy studies, the primary outcome was significant pain relief and the secondary outcome was a positive change in functional status. For the inclusion of the diagnostic controlled studies, all studies must have utilized either placebo controlled facet joint blocks or comparative local anesthetic blocks. In assessing therapeutic interventions, short-term and long-term reliefs were defined as either up to 6 mo or greater than 6 mo of relief. The literature search was extensive utilizing various types of electronic search media including PubMed from 1966 onwards, Cochrane library, National Guideline Clearinghouse, clinicaltrials.gov, along with other sources including

previous systematic reviews, non-indexed journals, and abstracts until March 2015. Each manuscript included in the assessment was assessed for methodologic quality or risk of bias assessment utilizing the Quality Appraisal of Reliability Studies checklist for diagnostic interventions, and Cochrane review criteria and the Interventional Pain Management Techniques - Quality Appraisal of Reliability and Risk of Bias Assessment tool for therapeutic interventions. Evidence based on the review of the systematic assessment of controlled studies was graded utilizing a modified schema of qualitative evidence with best evidence synthesis, variable from level I to level V.

RESULTS: Across all databases, 16 high quality diagnostic accuracy studies were identified. In addition, multiple studies assessed the influence of multiple factors on diagnostic validity. In contrast to diagnostic validity studies, therapeutic efficacy trials were limited to a total of 14 randomized controlled trials, assessing the efficacy of intraarticular injections, facet or zygapophysial joint nerve blocks, and radiofrequency neurotomy of the innervation of the facet joints. The evidence for the diagnostic validity of lumbar facet joint nerve blocks with at least 75% pain relief with ability to perform previously painful movements was level I, based on a range of level I to V derived from a best evidence synthesis. For therapeutic interventions, the evidence was variable from level II to III, with level II evidence for lumbar facet joint nerve blocks and radiofrequency neurotomy for long-term improvement (greater than 6 mo), and level III evidence for lumbosacral zygapophysial joint injections for short-term improvement only.

CONCLUSION: This review provides significant evidence for the diagnostic validity of facet joint nerve blocks, and moderate evidence for therapeutic radiofrequency neurotomy and therapeutic facet joint nerve blocks in managing chronic low back pain.

Key words: Chronic low back pain; Lumbar facet joint pain; Lumbar discogenic pain; Intraarticular injections; Lumbar facet joint nerve blocks; Lumbar facet joint radiofrequency; Controlled diagnostic blocks; Lumbar facet joint

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This review summarizes diagnostic and therapeutic aspects of chronic low back pain of facet joint origin. Even though multiple high quality diagnostic accuracy studies are available, there is room for further studies to confirm accuracy. These studies are key for the universal acceptance of facet joint nerve blocks of the lumbosacral spine as the gold standard. Deficiencies continue with therapeutic interventions. Lumbar radiofrequency neurotomy studies have shown contradicting results with short-term follow-ups. There is limited high quality literature for lumbar facet joint

nerve blocks, and the available literature contains contradictory findings in multiple trials of intraarticular injections.

Manchikanti L, Hirsch JA, Falco FJE, Boswell MV. Management of lumbar zygapophysial (facet) joint pain. *World J Orthop* 2016; 7(5): 315-337 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/315.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.315>

INTRODUCTION

Low back pain is a common health problem with increasing prevalence, health challenges, and economic impact^[1-20]. Studies indicate that low back pain is the number one cause contributing to most years lived with disability in 2010 in the United States and globally^[1,2]. In addition, work-related low back pain continues to be an important cause of disability^[3]. The global burden of low back pain has a point prevalence of 9.4% of the population, with severe chronic low back pain but a lack of lower extremity pain accounting for 17% of cases, and of low back pain with leg pain 25.8%^[2]. Low back pain increased 162% in North Carolina, from 3.9% in 1992 to 10.2% in 2006^[4]. Treatment of chronic low back pain has yielded mixed results and the substantial economic and health impact has raised concerns among the public-at-large, policy-makers, and physicians^[6-19]. The large increase in treatment types and rapid escalation in health care costs may be attributed to multiple factors, including the lack of an accurate diagnosis and various treatments that do not have appropriate evidence of effectiveness.

Numerous structures in the lower back may be responsible for low back and/or lower extremity pain, including lumbar intervertebral discs, facet joints, sacroiliac joints, and nerve root dura, and may be amenable to diagnostic measures such as imaging and controlled diagnostic blocks^[10,21-29]. Other structures also capable of transmitting pain, including ligaments, fascia, and muscles, may not be diagnosed with accuracy with any diagnostic techniques^[29]. Disc-related pathology with disc herniation, spinal stenosis, and radiculitis are diagnosed with reasonable ease and accuracy leading to definitive treatments^[30]. However, low back pain from discs (without disc herniation), lumbar facet joints, and sacroiliac joints is difficult to diagnose accurately by noninvasive measures including imaging^[10,21-35]. Consequently, no gold standard is generally acknowledged for diagnosing low back pain, irrespective of the source being facet joint(s), intervertebral disc(s), or sacroiliac joint(s), despite the fact that lumbar facet joints, the paired joints that stabilize and guide motion in the spine, have been frequently implicated.

Based on neuroanatomy, neurophysiologic, biomechanical studies, and controlled diagnostic facet joint nerve blocks, lumbar facet joints have been recognized

Table 1 Modified grading of qualitative evidence with best evidence synthesis for diagnostic accuracy and therapeutic interventions

Level I	Evidence obtained from multiple relevant high quality randomized controlled trials or Evidence obtained from multiple high quality diagnostic accuracy studies
Level II	Evidence obtained from at least one relevant high quality randomized controlled trial or multiple relevant moderate or low quality randomized controlled trials or Evidence obtained from at least one high quality diagnostic accuracy study or multiple moderate or low quality diagnostic accuracy studies
Level III	Evidence obtained from at least one relevant moderate or low quality randomized controlled trial study or Evidence obtained from at least one relevant high quality non-randomized trial or observational study with multiple moderate or low quality observational studies or Evidence obtained from at least one moderate quality diagnostic accuracy study in addition to low quality studies
Level IV	Evidence obtained from multiple moderate or low quality relevant observational studies or Evidence obtained from multiple relevant low quality diagnostic accuracy studies
Level V	Opinion or consensus of large group of clinicians and/or scientists.

Source: Manchikanti *et al.*^[82].

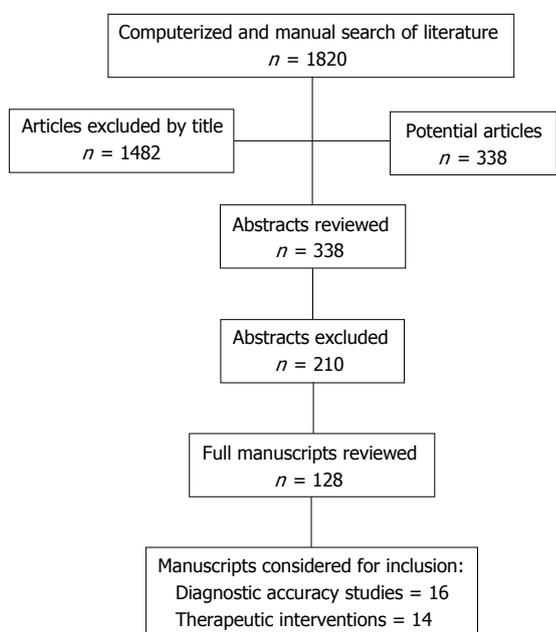


Figure 1 Flow diagram illustrating literature evaluating diagnostic accuracy and therapeutic effectiveness of lumbar facet joint interventions.

the criteria for inclusion for methodological quality assessment and then performed the methodological quality assessment. Authors with a perceived conflict of interest for any manuscript, either with authorship or any other aspect, were recused from reviewing those manuscripts.

For diagnostic accuracy studies, all articles were assessed based on the quality appraisal of reliability studies checklist, which has been validated^[80]. All randomized trials were assessed for methodological quality utilizing Cochrane review criteria^[78] and Inter-ventional Pain Management Techniques - Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria^[79].

Summary measures

Summary measures for diagnostic accuracy studies included at least 50% pain relief with an ability to perform previously painful movements as the criterion standard, whereas for RCTs, summary measures included a 50% or more reduction of pain in at least 40% of the patients or at least a 3 point decrease in pain scores.

Outcomes and analysis of evidence

Outcomes of the studies of diagnostic accuracy were assessed for prevalence and false-positive rates when available. For therapeutic efficacy, the short- and long-term outcomes were assessed. For diagnostic accuracy and therapeutic efficacy studies, 5 levels of evidence were utilized as shown in Table 1, varying from level I with the highest evidence with multiple relevant high quality RCTs, or multiple high quality diagnostic accuracy studies, to level V with minimal evidence and results based on consensus. Any disagreement among authors was resolved by a third author or by consensus.

RESULTS

Figure 1 lists the study selection flow diagram of diagnostic accuracy studies and therapeutic intervention trials.

Based on the search criteria, there were multiple diagnostic accuracy and therapeutic efficacy studies; however, utilizing inclusion criteria as described above, there were 16 diagnostic accuracy studies meeting inclusion criteria for methodological quality assessment^[22-25,84-95], whereas there were 14 trials meeting inclusion criteria for therapeutic efficacy assessment^[96-109]. Among the multiple trials not meeting methodological quality assessment inclusion criteria, Leclaire *et al.*^[110] was of significant importance. This trial was randomized and placebo controlled. It assessed 70 patients with a 12-wk follow-up. This was a relatively small study but

more importantly, the technique used was inappropriate as was using intraarticular injections for diagnostic evaluation. Subsequently, the authors have agreed that the results may not be applied in clinical practice^[111]. Multiple studies assessing the influence of factors of prevalence and accuracy of facet joint pain were also considered^[112-123].

Methodological quality assessment

Methodological quality assessment of diagnostic accuracy studies is shown in Table 2 and methodological quality assessment of therapeutic interventions by Cochrane review criteria is shown in Table 3, whereas methodological quality assessment utilizing IPM-QRB criteria is shown in Table 4.

Study characteristics

Diagnostic accuracy study characteristics are shown in Table 5, and therapeutic efficacy trial characteristics are shown in Table 6.

Among the diagnostic accuracy studies, 6 studies were performed utilizing $\geq 75\%$ pain relief as the criterion standard^[24,85-87,93,94]. All told there were 856 patients, a heterogenous population with prevalence ranging from 30% to 45%, including a false-positive rate of 25% to 44%. These results are also similar to 80% pain relief as the criterion standard studied in 5 studies^[23,89-91,95] in 1431 patients. The prevalence in a heterogenous population ranged between 27% and 41%. However, utilizing controlled diagnostic blocks, the prevalence was shown somewhat differently in specific populations with 30% in patients younger than 65 years and 52% in patients older than 65^[93], 36% in non-obese patients and 40% in obese patients^[94], 16% in post surgery patients^[92], and 21% with involvement of a single region^[88].

Among the therapeutic interventions, a total of 14 trials met inclusion criteria with 9 trials evaluating lumbar radiofrequency neurotomy^[96-101,105,108,109], 2 trials evaluating lumbar facet joint nerve blocks^[102,108], and 5 trials evaluating the role of intraarticular facet joint injections^[101,103,104,106,107]. Among the radiofrequency neurotomy trials, of the 9 trials included, 7 moderate to high quality trials showed long-term effectiveness^[96,98-101,105,108], whereas one moderate to high quality trial showed a lack of effectiveness^[97] with one trial showing short-term effectiveness^[109]. Among the long-term trials with effectiveness assessed at least for one year, Civelek *et al.*^[108] included 50 patients, Tekin *et al.*^[96] included 20 patients in the conventional radiofrequency neurotomy groups, and van Kleef *et al.*^[99] included only 15 patients in the radiofrequency neurotomy group showing positive results with a total number of 85 patients included among the 3 trials. van Wijk *et al.*^[97], showing a lack of effectiveness, included 40 patients undergoing radiofrequency neurotomy. Among the other studies, Cohen *et al.*^[109] included 14 patients with controlled diagnostic blocks, Nath *et al.*^[105] included 20 patients with triple diagnostic blocks, Dobrogowski *et*

al.^[98] included 45 patients with controlled diagnostic blocks, Moon *et al.*^[100] included 82 patients utilizing 2 different types of techniques with controlled diagnostic blocks, and Lakemeier *et al.*^[101] included 27 patients with an intraarticular injection of local anesthetic with a single block.

The evidence for therapeutic lumbar facet joint nerve blocks was assessed in 2 RCTs^[102,108]. In these trials, Manchikanti *et al.*^[102] studied 120 patients with chronic lumbar facet joint pain with a confirmed diagnosis with a criterion standard of 80% pain relief using controlled diagnostic blocks after failure of conservative management. At the end of a 2-year study period, significant pain relief was seen in 85% of the patients who received a local anesthetic and 90% of the patients who received a local anesthetic with steroids. The patients received an average of 5 to 6 total treatments. In the second study, Civelek *et al.*^[108] assessed 100 patients suffering from chronic low back pain. These patients had failed conservative therapy utilizing noninvasive diagnostic criteria; however, without diagnostic blocks. They compared lumbar facet joint nerve blocks with conventional radiofrequency neurotomy. Effectiveness was seen in 69% of the patients who received facet joint nerve blocks. In the radiofrequency neurotomy group, 90% effectiveness was seen. Civelek *et al.*^[108] showed significant improvement in 90% of the patients at one year follow-up, Cohen *et al.*^[109] showed 64% of the patients responding at 3 mo selected with controlled diagnostic blocks, Nath *et al.*^[105] showed at 6 mo follow-up significant reduction in the majority of patients, Tekin *et al.*^[96] reported a significant percentage of patients with appropriate relief at one year in the conventional radiofrequency neurotomy group, van Wijk *et al.*^[97] showed a lack of response at 3 mo follow-up, Dobrogowski *et al.*^[98] showed effectiveness of radiofrequency neurotomy in 66% of the patients at one year follow-up, van Kleef *et al.*^[99] showed effectiveness of radiofrequency neurotomy at one year in 47% of the patients, Moon *et al.*^[100] showed significant reduction in pain and disability index scores at the end of one year, and finally Lakemeier *et al.*^[101] showed significant improvement with conventional radiofrequency neurotomy at the end of 6 mo.

Intraarticular injections were studied in 5 trials^[101,103,104,106,107]. Of these, 3 high quality RCTs showed effectiveness with short-term follow-up of less than 6 mo^[101,106,107]. However, 2 moderate to high quality RCTs showed opposing results with a lack of effectiveness^[103,104]. Ribeiro *et al.*^[107] showed effectiveness of intraarticular injections at the end of 6 mo with selection criteria not including diagnostic blocks. Lakemeier *et al.*^[101] showed significant improvement with selection of patients with a single intraarticular injection at 6 mo. Yun *et al.*^[106] showed positive results at the end of 3 mo with selection of patients without diagnostic blocks. In contrast, Carrette *et al.*^[103] in a large controlled trial showed a lack of effectiveness of intraarticular steroid injections with selection of the patients with a single

Table 2 Quality appraisal of the diagnostic accuracy of lumbar facet joint nerve block diagnostic studies

	Manchikanti <i>et al.</i> ^[23]	Pang <i>et al.</i> ^[25]	Schwarzer <i>et al.</i> ^[22]	Schwarzer <i>et al.</i> ^[84]	Manchikanti <i>et al.</i> ^[86]	Manchikanti <i>et al.</i> ^[79]	Manchikanti <i>et al.</i> ^[85]	Manchikanti <i>et al.</i> ^[93]	Manchikanti <i>et al.</i> ^[94]	Manchikanti <i>et al.</i> ^[88]	Manchikanti <i>et al.</i> ^[82]	Manchikanti <i>et al.</i> ^[90]	Manchukonda <i>et al.</i> ^[91]	Manchikanti <i>et al.</i> ^[92]	Manchikanti <i>et al.</i> ^[95]	DePalma <i>et al.</i> ^[24]
(1) Was the test evaluated in a spectrum of subjects representative of patients who would normally receive the test in clinical practice?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
(2) Was the test performed by examiners representative of those who would normally perform the test in practice?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
(3) Were raters blinded to the reference standard for the target disorder being evaluated?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
(4) Were raters blinded to the findings of other raters during the study?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
(5) Were raters blinded to their own prior outcomes of the test under evaluation?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
(6) Were raters blinded to clinical information that may have influenced the test outcome?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
(7) Were raters blinded to additional cues, not intended to form part of the diagnostic test procedure?	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Table 3 Methodological quality assessment of randomized trials of lumbar facet joint interventions utilizing Cochrane review criteria

	Manchikanti <i>et al</i> ^[102]	Carette <i>et al</i> ^[103]	Fuchs <i>et al</i> ^[104]	Nath <i>et al</i> ^[105]	van Wijk <i>et al</i> ^[97]	van Kleef <i>et al</i> ^[99]	Tekin <i>et al</i> ^[95]	Cvelek <i>et al</i> ^[108]	Dobrogowski <i>et al</i> ^[98]	Cohen <i>et al</i> ^[109]	Ribeiro <i>et al</i> ^[107]	Moon <i>et al</i> ^[100]	Lakemeier <i>et al</i> ^[101]	Yun <i>et al</i> ^[106]
Randomization adequate	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concealed treatment allocation	Y	Y	N	Y	Y	Y	Y	Y	U	N	Y	Y	Y	Y
Patient blinded	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	N
Care provider blinded	Y	Y	N	Y	Y	Y	Y	N	Y	U	N	Y	N	N
Outcome assessor blinded	N	Y	Y	Y	Y	Y	Y	U	U	U	N	Y	N	N
Drop-out rate described	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
All randomized participants analyzed in the group	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Co-intervention avoided or similar in all groups	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Compliance acceptable in all groups	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y
Score	11/12	11/12	8/12	12/12	12/12	12/12	12/12	9/12	10/12	8/12	10/12	9/12	9/12	9/12

Y: Yes; N: No; U: Unclear. Source: Furlan *et al*^[98].

moderate to high quality randomized trials is level II with 7 trials^[96,98-101,105,108] showing efficacy for at least 6 mo follow-up, with discordant evidence demonstrating a lack of effectiveness in one moderate to high quality RCT^[97]. There is level II evidence for lumbar facet joint nerve blocks based on 2 moderate to high quality RCTs^[102,108] for long-term improvement. For lumbosacral intraarticular injections, the evidence is level III based on 3 RCTs^[101,106,107] showing effectiveness with 2 randomized trials showing a lack of effectiveness^[103,104].

In recent years, understanding lumbar facet joint pain, not only with pathophysiology, but with diagnostic and treatment strategies, has expanded with numerous publications^[10,15,22-25,34-49,53-55,84-123]. Hancock *et al*^[53] systematically assessed tests to identify the structures in the low back responsible for chronic pain, including facet joints. Their results demonstrated the lack of diagnostic accuracy for various tests. Thus, controlled diagnostic blocks seem to be the only viable and appropriate diagnostic method, despite discussions about the precision and accuracy of these techniques^[10,34]. Although the majority of systematic reviews demonstrate the accuracy of controlled diagnostic blocks when performed by interventional pain physicians^[10,28,34], others failed to demonstrate accuracy^[50-52] though debate continues^[10,28,34].

Rubinstein *et al*^[32] of the Cochrane Review Musculoskeletal Group conducted a best-evidence review of neck and low back pain diagnostic procedures. They concluded that surprisingly, many of the orthopedic tests for the low back had very little evidence to support their diagnostic accuracy in clinical practice. They also concluded that lumbar facet joint nerve blocks performed for diagnostic purposes had moderate evidence for their use. This was based on systematic reviews and diagnostic accuracy studies performed by interventional pain physicians prior to 2008. Since then, the literature has expanded considerably. As such, despite the fact that a true placebo control technique may be the gold standard, due to practical difficulties, such as limited clinical utility and cost implications, as well as the ethical and logistic issues associated with using a true placebo^[124-126], controlled comparative local anesthetic blocks with local anesthetics, both short-acting and long-acting, have become a recognized way for

Table 4 Methodological quality assessment of randomized trials utilizing Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment criteria

	Manchikanti <i>et al.</i> ⁽¹⁰²⁾	Carette <i>et al.</i> ⁽¹⁰³⁾	Fuchs <i>et al.</i> ⁽¹⁰⁴⁾	Nath <i>et al.</i> ⁽¹⁰⁵⁾	van Wijk <i>et al.</i> ⁽⁹⁷⁾	van Kleef <i>et al.</i> ⁽⁹⁹⁾	Tekin <i>et al.</i> ⁽⁹⁶⁾	Civelek <i>et al.</i> ⁽⁹⁸⁾	Dobrogowski <i>et al.</i> ⁽⁹⁸⁾	Cohen <i>et al.</i> ⁽¹⁰⁹⁾	Ribeiro <i>et al.</i> ⁽¹⁰⁷⁾	Moon <i>et al.</i> ⁽¹⁰⁰⁾	Lakemeier <i>et al.</i> ⁽¹⁰¹⁾	Yun <i>et al.</i> ⁽¹⁰⁶⁾
I Trial design and guidance reporting														
(1) Consort or spirit	3	3	3	3	2	2	2	2	2	3	2	2	2	2
II Design factors														
(2) Type and design of trial	2	3	2	3	3	3	3	2	2	2	2	2	2	2
(3) Setting/physician	2	1	1	3	3	3	2	2	2	2	2	2	1	1
(4) Imaging	3	3	2	3	3	3	3	3	2	3	3	3	3	3
(5) Sample size	3	2	2	1	1	1	1	1	1	3	2	2	2	2
(6) Statistical methodology	1	1	1	1	1	1	1	1	1	1	1	1	1	1
III Patient factors														
(7) Inclusiveness of Population														
For facet joint interventions:	2	1	0	2	1	1	1	0	1	1	0	2	1	0
(8) Duration of pain	2	2	1	2	2	3	2	0	2	0	0	2	2	0
(9) Previous treatments	2	0	0	0	0	0	1	2	0	0	0	2	2	1
(10) Duration of follow-up with appropriate interventions	3	2	1	2	2	2	2	2	1	0	1	1	2	1
IV Outcomes														
(11) Outcomes assessment criteria for significant improvement	4	4	2	4	4	2	2	2	2	0	2	2	2	1
(12) Analysis of all randomized participants in the groups	2	2	2	2	2	2	2	2	2	2	2	0	2	2
(13) Description of drop out rate	2	1	2	2	2	2	2	2	2	2	2	2	2	2
(14) Similarity of groups at baseline for important prognostic indicators	2	2	2	2	2	2	2	2	2	2	2	2	2	2
(15) Role of co-interventions	1	0	0	1	1	1	1	1	1	1	1	1	1	1
V Randomization														
(16) Method of Randomization	2	2	2	2	2	2	2	2	2	2	2	2	2	2
VI Allocation concealment														
(17) Concealed treatment allocation	2	2	1	2	2	2	2	2	2	0	2	2	2	2
VII Blinding														
(18) Patient blinding	1	1	0	1	1	1	1	0	1	0	1	1	1	0
(19) Care provider blinding	1	1	0	1	1	1	1	0	1	0	0	1	0	0
(20) Outcome assessor blinding	0	1	0	0	1	0	0	0	0	0	0	1	0	0
VIII Conflicts of interest														
(21) Funding and sponsorship	2	3	1	2	0	3	2	0	0	2	2	2	2	1
(22) Conflicts of interest	3	3	1	3	0	3	2	0	0	2	3	3	3	0
Total	45	40	26	42	36	40	37	28	29	28	32	32	38	37

Source: Manchikanti *et al.*⁽⁹⁹⁾.

diagnosing chronic lumbar facet joint pain, without disc herniation or radicular pain, after failing conservative management. Once the diagnosis is established, patients may be offered treatment with lumbar facet joint nerve blocks or radiofrequency neurotomy, and perhaps intraarticular facet injections.

Significant progress also has been made with therapeutic interventions, according to RCTs and systematic reviews published over the past 5 years. Consequently, the quality and level of evidence for therapeutic interventions has been improving, with level II evidence for long-term relief (longer than 6 mo) for radiofrequency neurotomy and therapeutic lumbar facet joint nerve blocks, even though the evidence for lumbosacral intraarticular injections continues to lack for long-term improvement and is level III for short-term improvement.

There has been substantial controversy in reference to technique. Bogduk *et al.*⁽⁷¹⁾ have recommended parallel placement of the needle to achieve appropriate results

Table 5 Characteristics of studies assessing the accuracy of diagnostic facet joint injections and nerve blocks in the lumbar spine					
Study/methods Methodological quality scoring	Participants	Intervention(s)	Outcome measures	Comments	Results Prevalence with 95%CI and criterion standard False-positive rate with 95%CI
Pang <i>et al.</i> ^[25] , 1998 Prospective, single block 8/12	100 consecutive adult patients with chronic low back pain with undetermined etiology were evaluated with spinal mapping	Single block was performed by injecting 2% lidocaine into facet joints	Verbal analog scale Pain mapping 90% pain relief	This is the first study evaluating application of diagnostic blocks in the diagnosis of intractable low back pain of undetermined etiology with facet joint disease in potentially 48% of patients with a single block	Single block: 90% pain relief Only facet joint pain = 24% Lumbar nerve root and facet disease = 24% Total = 48% NA
Schwarzer <i>et al.</i> ^[23] , 1994 Prospective, controlled diagnostic blocks 9/12	176 consecutive patients with chronic low back pain after some type of injury	Zygapophysial joint nerve blocks or intraarticular injections were performed with either 2% lignocaine or 0.5% bupivacaine	At least 50% pain relief concordant with the duration of local anesthetic injected	First study of evaluation of controlled prevalence and false-positive rates	50% pain relief 15% (95%CI: 10%-20%) 38% (95%CI: 30%-46%)
Schwarzer <i>et al.</i> ^[61] , 1995 Randomized, impure placebo, controlled diagnostic blocks 9/12	63 patients with low back pain lasting for longer than 3 mo underwent computed tomography and blocks of the zygapophysial joints	Patients underwent a placebo injection followed by intraarticular zygapophysial joint injections with 1.5 mL of 0.5% bupivacaine	At least 50% reduction in pain maintained for minimum of 3 h	This study shows that computed tomography has no place in the diagnosis of lumbar zygapophysial joint pain, with an impure placebo design	50% pain relief 40% (95%CI: 27%-53%) NA
Manchikanti <i>et al.</i> ^[65] , 2010 Retrospective, controlled diagnostic blocks 9/12	491 patients with chronic low back pain undergoing evaluation for facet joint pain with 80% pain relief and 181 patients with 50% pain relief	Controlled diagnostic blocks of lumbar facet joint nerves with 1% preservative-free lidocaine and 0.25% preservative-free bupivacaine 1 mL	At least 80% pain relief with the ability to perform previously painful movements	Higher prevalence than with 50% pain relief, but still higher than double block algorithmic approach	50% pain relief 61% (95%CI: 53%-81%) 17% (95%CI: 10%-24%) 80% pain relief
Manchikanti <i>et al.</i> ^[65] , 2000 Prospective, controlled diagnostic blocks 9/12	200 consecutive patients with chronic low back pain were evaluated	Controlled diagnostic blocks with 1% lidocaine and 0.25% bupivacaine were injected over facet joint nerves with 0.4 to 0.6 mL	75% pain relief with ability to perform previously painful movements	The study showed that the clinical picture failed to diagnose facet joint pain	31% (95%CI: 26%-35%) 75% pain relief 42% (95%CI: 35%-42%) 80% pain relief 42% (95%CI: 35%-50%) 37% (95%CI: 32%-42%)
DePalma <i>et al.</i> ^[26] , 2011 Retrospective, controlled diagnostic blocks 9/12	A total of 156 patients with chronic low back pain were assessed for the source of chronic low back pain including discogenic pain, facet joint pain and sacroiliac joint pain	Dual controlled diagnostic blocks with 1% lidocaine for the first block with 0.5% bupivacaine for the second	Concordant relief with 2 h for lidocaine and 8 h for bupivacaine with 75% pain relief as the criterion standard	This is the third study evaluating various structures implicated in the cause of low back pain with controlled diagnostic blocks ^[21,23]	75% pain relief 31% (24%-38%) NA
Manchikanti <i>et al.</i> ^[65] , 2001 Prospective, controlled diagnostic blocks 9/12	Prevalence study in 100 patients with 50 patients below age of 65 and 50 patients aged 65 or over was assessed	Controlled diagnostic blocks	75% pain relief with ability to perform previously painful movements was utilized as the criterion standard	This study showed higher prevalence of facet joint pain in the elderly compared to the younger age group in contrast to the latest study by Manchikanti <i>et al.</i> ^[17] which showed no differences	75% pain relief < 65 yr = 26% (95%CI: 11%-40%) > 65 yr = 33% (95%CI: 17%-43%) 52% (95%CI: 38%-66%) 14%-35%
Manchikanti <i>et al.</i> ^[64] , 2001 Prospective, controlled diagnostic blocks 9/12	100 patients with low back pain were evaluated. Patients were divided into 2 groups: group I was normal weight and group II was obese	Facet joints were investigated with diagnostic blocks using lidocaine 1% initially followed by bupivacaine 0.25%, at least 2 wk apart	A definite response was defined as relief of at least 75% in the symptomatic area	This study showed no significant difference between obese and non-obese individuals either with prevalence or false-positive rate of diagnostic blocks in chronic facet joint pain	75% pain relief Non-obese individuals = 44% (95%CI: 26%-61%) Obese individuals = 36% (95%CI: 16%-51%) Prevalence: Non-obese individuals = 36% (95%CI: 22%-50%) Obese individuals = 40% (95%CI: 26%-54%)

Manchikanti <i>et al</i> ^[83] , 2001 Prospective, controlled diagnostic blocks 9/12	120 patients were evaluated with chief complaint of chronic low back pain to evaluate relative contributions of various structures in chronic low back pain. All 120 patients underwent facet joint nerve blocks	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	80% pain relief with ability to perform previously painful movements	This study evaluated all the patients with low back pain, even with suspected discogenic pain	80% pain relief 40% (95%CI: 31%-49%)	47% (95%CI: 35%-59%)
Manchikanti <i>et al</i> ^[84] , 1999 Prospective, controlled diagnostic blocks 9/12	120 patients with chronic low back pain after failure of conservative management were evaluated	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	Concordant pain relief with 75% or greater criterion standard with ability to perform previously painful movements	This was the first study performed in the United States in the heterogeneous population as previous studies were performed in only post-injury patients	75% pain relief 45% (95%CI: 36%-54%)	41% (95%CI: 29%-53%)
Manchikanti <i>et al</i> ^[79] , 2014 Prospective, controlled diagnostic blocks 9/12	180 consecutive patients with chronic low back pain were evaluated after having failed conservative management	Controlled diagnostic blocks with 1% lidocaine and 0.25% bupivacaine with or without Sarapain and/or steroids	75% pain relief with ability to perform previously painful movements	This study showed no significant difference if the steroids were used or not	75% pain relief 36% (95%CI: 29%-43%)	25% (95%CI: 21%-39%)
Manchikanti <i>et al</i> ^[85] , 2003 Prospective, controlled diagnostic blocks 9/12	At total of 300 patients with chronic low back pain were evaluated to assess the difference based on involvement of single or multiple spinal regions	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	80% pain relief with ability to perform previously painful movements	This study shows a higher prevalence when multiple regions are involved	80% pain relief Single region: 17% (95%CI: 10%-24%) Multiple regions: 21% (95%CI: 14%-27%) 41% (95%CI: 33%-49%)	Single region: 17% (95%CI: 10%-24%) Multiple regions: 27% (95%CI: 18%-36%)
Manchikanti <i>et al</i> ^[83] , 2014 Prospective, controlled diagnostic blocks 9/12	120 consecutive patients with chronic low back pain and neck pain were evaluated to assess involvement of facet joints as causative factors	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	80% pain relief with ability to perform previously painful movements	The results are similar to involvement of multiple regions with a prevalence of 40% as illustrated in another study	80% pain relief 40% (95%CI: 31%-49%)	30% (95%CI: 20%-40%)
Manchikanti <i>et al</i> ^[90] , 2004 Prospective, controlled diagnostic blocks 9/12	500 consecutive patients with chronic, non-specific spinal pain were evaluated of which 397 patients suffered with chronic low back pain	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	80% pain relief with ability to perform previously painful movements	Largest study performed involving all regions of the spine	80% pain relief 31% (95%CI: 27%-36%)	27% (95%CI: 22%-32%)
Manchukonda <i>et al</i> ^[91] , 2007 Retrospective, controlled diagnostic blocks 9/12	500 consecutive patients with chronic spinal pain were evaluated of which 303 patients were evaluated for chronic low back pain	Controlled diagnostic blocks with 1% lidocaine followed by 0.25% bupivacaine	80% pain relief with ability to perform previously painful movements	Second largest study performed involving all regions of the spine	80% pain relief 27% (95%CI: 22%-33%)	45% (95%CI: 36%-53%)
Manchikanti <i>et al</i> ^[83] , 2007 Prospective, controlled diagnostic blocks 9/12	A total of 117 consecutive patients with chronic non-specific low back pain were evaluated, after lumbar surgical interventions, with postsurgery syndrome and continued axial low back pain	Controlled, comparative, local anesthetic blocks with 1% lidocaine and 0.25% bupivacaine	80% relief as the criterion standard with ability to perform previously painful movements	Lower prevalence in postsurgery patients	80% pain relief 16% (95%CI: 9%-23%)	49% (95%CI: 39%-59%)

NA: Not applicable.

Table 6 Study characteristics of randomized controlled trials of lumbar radiofrequency neurotomy, facet joint nerve blocks, and intraarticular injections

Study/study characteristic/ methodological quality Scoring	No. of patients and selection criteria	Control	Interventions	Outcome measures	Time of measurement	Reported results	Strengths	Weaknesses	Conclusion/ comments
Radiofrequency neurotomy Civelek <i>et al</i> ^[108] , 2012 Randomized, active-control trial Quality scores: Cochrane = 9/12 IPM-QRB = 28/48	100 patients with chronic low back pain with failed conservative therapy and strict selection criteria; however, without diagnostic blocks	Facet joint nerve block with local anesthetic and steroids in 50 patients	Conventional radiofrequency neurotomy at 80 °C for 120 s in combination with high dose local anesthetic and steroids, in 50 patients	Visual Numeric Pain Scale, North American Spine Society patient satisfaction questionnaire, Euro-Qol in 5 dimensions and ≥ 50% relief	1, 6 and 12 mo	At one year, 90% of patients in the radiofrequency group and 69% of the patients in the facet joint nerve block group showed significant improvement compared to 92% and 75% at 6-mo follow-up	Randomized relatively large number of patients with 50 in each group and local anesthetics were utilized in both groups	No diagnostic blocks were performed. High dose steroids and local anesthetics were utilized in both groups	Efficacy was shown even without diagnostic blocks, both for facet joint nerve blocks and radiofrequency neurotomy
Cohen <i>et al</i> ^[109] , 2010 Randomized, double-blind, control trial Quality scores: Cochrane = 8/12 IPM-QRB = 28/48	151 chronic low back pain, 51 patients with no diagnostic block, 50 patients a single diagnostic block, 50 patients in double diagnostic block	Radiofrequency neurotomy in patients without diagnostic blocks	Conventional radiofrequency neurotomy at 80 °C for 90 s in all patients; however, in 2 groups with either a single block paradigm or a double block paradigm testing for positive results	Greater than 50% pain relief coupled with a positive global perceived effect persisting for 3 mo	3 mo	Denervation success rates in groups 0, 1 and 2 were 33%, 39% and 64%, respectively	Multicenter, randomized controlled trial with or without diagnostic blocks	Authors misinterpreted cost- effectiveness without consideration of many factors reported	Results showed efficacy when double diagnostic blocks were utilized
Nath <i>et al</i> ^[103] , 2008 Randomized, double-blind, sham control trial Quality scores: Cochrane = 12/12 IPM-QRB = 42/48	40 patients with chronic low back pain for at least 2 yr with 80% relief of low back pain after controlled medial branch blocks. The patients were randomized into an active and a control group	Controlled sham lesion in 20 patients in the control group	The 20 patients in the active group received conventional lumbar facet joint radiofrequency neurolysis at 85 °C for 60 s. The 20 patients in the control group received sham treatment without radiofrequency neurolysis of the lumbar facet joints	Numeric Rating Scale, global functional improvement, reduced opioid intake, employment status	6 mo	Significant reduction not only in back and leg pain; functional improvement; opioid reduction; and employment status in the active group compared to the control group	Randomized, double- blind trial after the diagnosis of facet joint pain with triple diagnostic blocks	Short-term follow-up with small number of patients	Efficacy of radiofrequency neurotomy was shown compared to local anesthetic injection and sham lesioning
Tekin <i>et al</i> ^[60] , 2007 Randomized, active and sham, double-blind controlled trial Quality scores: Cochrane = 12/12 IPM-QRB = 37/48	60 patients with chronic low back pain randomized into 3 groups with 20 patients in each group. Single diagnostic block of facet joint nerves with 0.3 mL of lidocaine 2% with	Sham control with local anesthetic injection	Either pulsed radiofrequency (42 °C for 4 min) or conventional radiofrequency neurotomy (80 °C for 90 s) in 20 patients in each group	Visual analog scale and Oswestry Disability Index	3, 6 and 12 mo	Visual analog scale and Oswestry Disability Index scores decreased in all groups from 3 procedural levels. Decrease in pain scores was maintained in the conventional radiofrequency group at also utilized a parallel 6 mo and one year.	Randomized, double- blind, controlled trial comparing control, pulsed radiofrequency, and conventional radiofrequency neurotomy. Authors also utilized a parallel needle placement	Small sample size with a single block and 50% relief as inclusion criteria. Authors have not described the significant improvement percentages	Efficacy with conventional radiofrequency neurotomy up to one year, whereas efficacy with local anesthetic block with sham control radiofrequency neurotomy and

	50% or greater relief			However, in pulsed radiofrequency group, the improvement was significant only at 6 mo, but not 1 yr	approach	pulsed radiofrequency neurotomy at 6 mo only
van Wijk <i>et al.</i> ⁽⁹⁷⁾ , 2005 Randomized, double-blind, sham control trial Quality scores: Cochrane = 12/12 IPM-QRB = 36/48	81 patients with chronic low back pain were evaluated with radiofrequency neurotomy with 41 patients in the control group with at least 50% relief for 30 min with a single block with intraarticular injection of 0.5 mL lidocaine 2%	Sham lesion procedure after local anesthetic injection	40 patients received conventional radiofrequency lesioning at 80 °C for 60 s and 41 patients received sham lesioning	Pain relief, physical activities, analgesic intake, global perceived effect, short-form-36, quality of life measures	Double-blind, sham control, randomized trial	Lack of efficacy with methodological deficiencies and a short-term follow-up
Dobrogowski <i>et al.</i> ⁽⁹⁸⁾ , 2005 Randomized, active control trial Quality scores: Cochrane = 10/12 IPM-QRB = 29/48	45 consecutive patients with chronic low back pain judged to be positive with controlled diagnostic blocks	Injection of saline in patients after conventional radiofrequency (85 °C for 60 s) neurotomy to evaluate postoperative pain	Conventional radiofrequency neurotomy at 85 °C for 60 s, followed by injection of either methylprednisolone or pentoxifylline	Visual analog scale, minimum of 50% reduction of pain intensity, patient satisfaction score	Randomized, active control trial	Radiofrequency neurotomy effective with or without steroid injection after neurolysis
van Kleef <i>et al.</i> ⁽⁹⁹⁾ , 1999 Randomized, double-blind, sham control trial Quality scores: Cochrane = 12/12 IPM-QRB = 40/48	31 patients with a history of at least one year of chronic low back pain randomly assigned to one of 2 treatment groups. Single diagnostic block with 50% relief	Sham control of radiofrequency after local anesthetic injection in 16 patients	The 15 patients in the conventional radiofrequency treatment group received an 80 °C radiofrequency lesion for 60 s	Visual analog scale, pain scores, global perceived effect, Oswestry Disability Index	Double-blind, randomized, sham controlled trial	Efficacy shown in a small sample with a single diagnostic block

Moon <i>et al</i> ^[100] , 2013	Prospective, randomized, comparative study	Quality scores: Cochrane = 9/12 IPM-QRB = 38/48	82 patients were included with low back pain with 41 patients in each group either with a parallel placement of the needle or perpendicular placement of the needle	An active control trial with needle placement with perpendicular approach	41 patients in each group were treated with radiofrequency (80 °C for 90 s) after appropriate diagnosis of facet joint pain with dual diagnostic blocks with 50% relief as the criterion standard. The needle was positioned either utilizing a discal approach or perpendicular or utilizing tunnel vision approach with parallel placement of the needle	NRS, ODI	1 and 6 mo	Patients in both groups showed a statistically significant reduction in NRS and Oswestry disability index scores from baseline to that of the scores at 1 and 6 mo (all <i>P</i> < 0.0001, Bonferroni corrected)	Randomized, double-blind, controlled trial. The major strength is that authors have proven that parallel approach may not be the best as has been described. Diagnosis of facet joint pain by dual blocks	Active controlled trial without placebo group. Short-term follow-up	Positive results in an active controlled trial, in a relatively short-term follow-up of 6 mo, with positioning of the needle either with distal approach (perpendicular placement or tunnel vision) with parallel placement of the needle with some superiority with perpendicular approach. This trial abates any criticism of needle positioning one way or the other and the traditional needle positioning appears to be superior to parallel needle placement	
Lakemeier <i>et al</i> ^[101] , 2013	Randomized, double-blind, active controlled trial	Quality scores: Cochrane = 9/12 IPM-QRB = 37/48	56 patients were randomized into 2 groups with 29 patients receiving intraarticular steroid injections and 27 patients receiving radiofrequency denervation after the diagnosis was made with intraarticular injection of local anesthetic with a single block	Intraarticular injection of local anesthetic and steroid	Radiofrequency neurotomy for 90 s at 80 °C	Roland-Morris questionnaire, VAS, ODI, analgesic intake	6 mo	Pain relief and functional improvement were observed in both groups. There were no significant differences between the 2 groups for pain relief and functional status improvement	Lack of placebo group. Relatively short-term follow-up	Randomized, double-blind trial with single diagnostic block with intraarticular injection	Both groups showed improvement. Effectiveness at 6 mo in both groups with intraarticular injection or radiofrequency neurotomy	
Lumbar facet joint nerve blocks												
Civelek <i>et al</i> ^[108] , 2012	Randomized, active-control trial	Quality scores: Cochrane = 9/12 IPM-QRB = 28/48	100 patients with chronic low back with failed conservative therapy and strict selection criteria; however, without diagnostic blocks	Blocks of facet joint nerves with local anesthetic and steroids	Conventional radiofrequency neurotomy at 80 °C for 120 s in combination with high dose local anesthetic and steroids	Visual Numeric Pain Scale, North American Spine Society patient satisfaction questionnaire, Euro-Qol in 5 dimensions and \geq 50% relief	1, 6 and 12 mo	At the end of one year, 90% of patients in the radiofrequency group and 69% of the patients in the facet joint nerve block group showed significant improvement vs 92% and 75% at 6-mo follow-up	Randomized active-control trial with relatively large number of patients with 50 in each group	No diagnostic blocks were performed. High dose steroids and local anesthetics were provided in both groups	Results showed efficacy even without diagnostic blocks, both for facet joint nerve blocks and radiofrequency neurotomy	

<p>Manchikanti <i>et al</i>^[06], 2010 Randomized, double blind, active control trial Quality scores: Cochrane = 11/12 IPM-QRB = 45/48</p>	<p>120 patients with chronic low back pain of facet joint origin treated with therapeutic lumbar facet joint nerve blocks Double diagnostic blocks with 80% relief</p>	<p>Local anesthetic only</p>	<p>Total of 120 patients with 60 patients in each group with local anesthetic alone or local anesthetic and steroids. Both groups were also divided into 2 categories each with the addition of Sarapin</p>	<p>Numeric Rating Scale, Oswestry Disability Index, employment status, and opioid intake</p>	<p>3, 6, 12, 18 and 24 mo</p>	<p>Significant pain relief was shown in 85% in local anesthetic group and 90% in local anesthetic with steroids group at the end of the 2 yr study period in both groups, with an average of 5-6 total treatments</p>	<p>Randomized trial with relatively large proportion of patients with 2-yr follow-up, with inclusion of patients diagnosed with controlled diagnostic blocks</p>	<p>Lack of placebo group</p>	<p>Effectiveness demonstrated with facet joint nerve blocks with local anesthetic with or without steroids</p>
<p>Lumbar intraarticular injections Carette <i>et al</i>^[03], 1991 Randomized, double blind, impure placebo or active-control trial Quality scores: Cochrane = 11/12 IPM-QRB = 40/48</p>	<p>Patients with chronic low back pain who reported immediate relief of their pain after injection of local anesthetic into the facet joints. Single diagnostic blocks with 50% relief were randomly assigned to receive injections under fluoroscopic guidance</p>	<p>Intraarticular injection of isotonic saline</p>	<p>Injection of either sodium chloride or methylprednisolone into the facet joints (49 for isotonic saline and 48 for sodium chloride). Only one injection was provided</p>	<p>Visual Analog Scale, McGill Pain Questionnaire, mean sickness impact profile</p>	<p>1, 3 and 6 mo</p>	<p>After 1 mo, 42% of the patients in the methylprednisolone group and 33% in the sodium chloride group reported marked or very marked improvement. At the 6 mo evaluation, 46% in the methylprednisolone group and 15% in the placebo group showed sustained relief. Revised statistics showed 22% improvement in active group and 10% in control group</p>	<p>Well-performed randomized, double-blind controlled trial</p>	<p>Only single block was applied and patients were treated with steroids without local anesthetic with only one treatment and expected 6 mo of relief</p>	<p>The authors concluded that results were negative in an active-control trial with injection of either sodium chloride solution or steroid into the facet joints after diagnosis with a single block</p>
<p>Fuchs <i>et al</i>^[04], 2005 Randomized, double-blind, active-control trial Quality scores: Cochrane = 8/12 IPM-QRB = 26/48</p>	<p>60 patients with chronic low back pain were included with patients randomly assigned into 2 groups. No diagnostic blocks</p>	<p>Active-control study with no control group</p>	<p>Intraarticular injection of hyaluronic acid vs glucocorticoid injection</p>	<p>VAS, Rowland-Morris Questionnaire, ODI, low back outcomes score, short form-36</p>	<p>3 and 6 mo</p>	<p>Patients reported lasting pain relief, better function, and improved quality of life with both treatments</p>	<p>Randomized, active-control, double-blind study</p>	<p>Relatively small sample of patients with 6 mo follow-up without a placebo group, without diagnostic blocks</p>	<p>Undetermined (clinically inapplicable) results with high number of injections during a 6-mo period</p>
<p>Ribeiro <i>et al</i>^[07], 2013 Randomized, double-blind, active control Quality scores: Cochrane = 10/12 IPM-QRB = 32/48</p>	<p>60 patients with a diagnosis of facet joint syndrome randomized into experimental and control groups</p>	<p>Triamcinolone acetamide intramuscular injection of 6 lumbar paravertebral points</p>	<p>Intraarticular injection of 6 lumbar facet joints with triamcinolone hexacetamide</p>	<p>Pain visual analogue scale, pain visual analogue scale during extension of the spine, Likert scale, improvement percentage scale, Roland-Morris, 36-Item Short Form Health Survey, and</p>	<p>1, 4, 12 and 24 wk</p>	<p>Both groups showed improvement with no statistical difference between the groups. Improvement "percentage" analysis at each time point showed significant differences between the groups at week 7 and week 12. Improvement percentage was > 50% at all times in the</p>	<p>Randomized, double-blind controlled trial</p>	<p>Diagnostic blocks were not employed, thus, many patients without facet joint pain may have been included in this trial</p>	<p>Overall intraarticular steroids showed positive effectiveness for 24 wk compared to intramuscular steroids provided in a double-blind manner</p>

Lakemeier <i>et al.</i> ^[101] , 2013 Randomized, double-blind, active controlled trial Quality scores: Cochrane = 9/12 IPM-QRB = 37/48	56 patients were randomized into 2 groups receiving intraarticular steroid injections or radiofrequency denervation after the diagnosis was made with intraarticular injection of local anesthetic with a single block	Intraarticular injection of local anesthetic and steroid in 29 patients	Radiofrequency neurotomy for 90 s at 80 °C in 27 patients	Roland-Morris questionnaire, VAS, ODI, analgesic intake	6 mo	Pain relief and functional improvement were observed in both groups. There were no significant differences between the 2 groups for pain relief and functional status improvement	Lack of placebo group. Relatively short-term follow-up with intraarticular injection	Randomized, double-blind trial with single diagnostic block with intraarticular injection	Both groups showed improvement. Effectiveness of both modalities at 6 mo in both groups
Yun <i>et al.</i> ^[106] , 2012 Randomized, active controlled trial Quality scores: Cochrane = 9/12 IPM-QRB = 26/48	57 patients with facet syndrome were assigned to 2 groups with 32 patients in the fluoroscopy group and 25 patients in the under ultrasonography group without diagnostic blocks	Intraarticular injection of lidocaine and triamcinolone under fluoroscopic guidance	Intraarticular injection of lidocaine and triamcinolone under ultrasonic guidance	VAS, physician's and patient's global assessment (PhyGA, PaGA), modified ODI	1 wk, 1 and 3 mo	Each group showed significant improvement from the facet joint injections. However at a week, a mo, and 3 mo after injections, no significant differences were observed between the groups	Randomized trial	Short-term follow-up with no diagnostic blocks, thus increasing the potential for inclusion of patients without facet joint pain. The aim of study mainly was to confirm if ultrasonic imaging was appropriate	The study showed positive results in both groups with intraarticular steroid injections with a short-term follow-up whether performed under ultrasonic guidance or fluoroscopy

IPM-QRB: Interventional Pain Management Techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; VAS: Visual analog scale; ODI: Oswestry Disability Index.

with conventional radiofrequency neurotomy. However, an analysis of results shows no significant difference in outcomes with placement of the needle, either parallel or perpendicular. In fact, Moon *et al.*^[100], in a prospective randomized comparative trial of 82 patients, showed improvement to be equal in both groups. The selection criteria were dual diagnostic blocks with 50% relief. Dobrogowski *et al.*^[98] compared 45 consecutive patients in a randomized active-control trial studying the role of methylprednisolone or pentoxifylline after performing conventional radiofrequency neurotomy. The results were similar in both groups without any significant influence of methylprednisolone. The study essentially looked at postoperative pain relief with steroids after conventional radiofrequency neurotomy. Cohen *et al.*^[109] assessed the efficacy of radiofrequency neurotomy with a 3 mo follow-up with either no diagnostic blocks, single diagnostic block, or dual diagnostic blocks. The results were superior in patients selected after dual diagnostic blocks, with 64% responding; whereas in patients without a diagnostic block, the response rate was 33% and in the group with a single diagnostic block, the response rate was 39%. Civelek *et al.*^[108] performed conventional radiofrequency neurotomy in 50 patients without first performing any diagnostic blocks with significant improvement in 90% of patients at the end of one year. Nath *et al.*^[105], in a randomized double-blind sham control trial with a 6 mo follow-up, showed effectiveness of conventional radiofrequency neurotomy compared to sham lesioning and local anesthetic injection. The 2 RCTs assessing facet joint nerve blocks showed positive results in 69% of the patients by Civelek *et al.*^[108] and 90% of the patients by Manchikanti *et al.*^[102] with local anesthetic alone or with local anesthetic and steroids (85% in the local anesthetic group and 90% in the local anesthetic with steroids group) at the end of a 2-year period. However, lumbosacral intraarticular injections did not produce

convincing positive results, with some benefit on a short-term basis in 3 cases^[101,106,107] and 2 trials^[103,104] showing no response.

Even now, there remains significant controversy regarding the diagnostic accuracy and therapeutic efficacy of facet procedures, particularly in reference to interventional techniques, including escalating utilization patterns and costs^[6,10,13,14,68,127]. In fact, in the United States, the Office of Inspector General of the Department of Health and Human Services conducted an assessment of the appropriateness of facet joint injections, concluding that many of the procedures were inappropriate, without medical necessity and indications^[117]. Further, in the current regulatory atmosphere, many local coverage determinations may paradoxically increase the utilization of facet joint interventions^[68]. The present data show that facet joint interventions have increased 293% per 100000 fee-for-service (FFS) Medicare population from 2000 to 2013, with an increase of 213% for lumbar facet joint interventions and a 522% for lumbosacral facet neurolysis. Likewise, there has been an increase in cervical and thoracic facet joint nerve blocks of 350%, and an increase in facet neurolysis of 845% from 2000 to 2013 in the FFS population^[6,13,14,68]. However, the lumbar procedure increases appear to be smaller than cervical and thoracic facet joint interventions, even though the absolute procedure numbers are much higher for lumbar facet joint interventions. These data reflect only FFS Medicare patients in the United States, thus increases could be even higher.

There has been substantial discussion about various treatment strategies, control design of trials, placebo and nocebo effects, outcomes assessment between 2 active treatments rather than baseline to follow-up period, and ever-changing methodological quality assessment^[10,15,50,51,55,128,129]. For interventional techniques, complex mechanisms and variations in placebo and nocebo responses have been well described^[123-126,128-133]. Thus far, appropriately designed placebo studies, *i.e.*, injecting inactive solutions into inactive structures, have shown substantially accurate results without significant placebo effect^[134,135]. Further, it is crucial to note that most investigators are missing the role of the nocebo effect^[123-126]. Thus, clinical trials must be designed appropriately with clinical relevance to avoid erroneous conclusions. Further, many studies have used subacute or acute patients without standard conservative management.

The results of this systematic review are similar to the results of numerous other systematic reviews^[10,28,51,54,55,69-73]; however, they do not agree with the systematic reviews of others^[15,50]. Systematic reviews that showed a lack of effectiveness were often based on flawed methodology, also utilized in RCTs^[136-144]. Our results are similar to those of Falco *et al.*^[28,54] even though we used stricter criteria for the methodological quality assessment. In addition, in a systematic review of the comparative effectiveness of different solutions, including local anesthetics and steroids, Manchikanti *et*

al.^[136] showed equal efficacy of local anesthetic compared to steroids in long-term follow-up of lumbar facet joint nerve blocks; lumbar intraarticular facet injections were not found to be effective.

This evaluation included only RCTs for efficacy assessment, thus it can be argued that we missed many high quality observational studies^[71,144]. However, with adequate randomized trials available for radiofrequency neurotomy and intraarticular injections, inclusion of observational studies would not alter the findings.

The current study illustrates the diagnostic value and validity of nerve blocks and the therapeutic effectiveness of facet joint interventions, specifically radiofrequency neurotomy and facet joint nerve blocks for managing lumbar spine pain. Sixteen diagnostic accuracy studies and 14 RCTs of therapeutic interventions demonstrated level I evidence for using lumbar facet joint nerve blocks as a diagnostic tool for chronic low back pain, level II evidence for the therapeutic benefit of radiofrequency neurotomy and facet joint nerve blocks for long-term improvement (longer than 6 mo), and level III evidence with lumbosacral intraarticular injections for short-term improvement. Despite the debate regarding appropriate use of therapeutic modalities in managing lumbar facet joint pain, the accuracy of diagnostic facet joint nerve blocks and the efficacy of therapeutic facet joint interventions are supported by high-quality evidence for appropriately selected patients after failure of conservative treatment.

ACKNOWLEDGMENTS

Drs. Manchikanti, Hirsch, Falco, and Boswell contributed to this work. Drs. Manchikanti and Boswell designed the research; Drs. Manchikanti and Falco performed the research; Drs. Manchikanti and Hirsch contributed new reagents/analytic tools; Drs. Manchikanti and Hirsch analyzed the data; Drs. Manchikanti and Hirsch wrote the paper. All authors reviewed all contents and approved for submission.

COMMENTS

Background

In this systematic review, the diagnostic validity and therapeutic value of lumbar facet joint interventions in managing chronic low back pain were performed. Facet joint interventions are one of the multitude of modalities in managing chronic low back pain without disc herniation. There is a paucity of literature of not only systematic reviews, but also randomized controlled trials (RCTs) describing the efficacy of various modalities utilized and also diagnostic validity with controlled diagnostic blockade.

Research frontiers

There is a paucity of literature in assessing the diagnostic capability of various non-interventional and interventional modalities including radiologic investigations. Due to a lack of validity of various types of investigations, controlled diagnostic blocks have been considered as a reliable method in arriving at the diagnosis of facet joint pain. Similarly, there is also a paucity of literature in reference to therapeutic efficacy of various types of facet joint interventions utilized in managing chronic low back pain including intraarticular injections, facet joint nerve blocks, and radiofrequency neurotomy. By the same

token, there is also a paucity of systematic reviews assessing the value and validity of diagnostic and therapeutic facet joint interventions in the lumbar spine.

Innovations and breakthroughs

The previous systematic reviews have limited their assessment to either diagnostic or therapeutic validity and value. Further, assessment has been carried utilizing variable methodologic quality assessments. In this systematic review, the authors have utilized the most recent methodologic quality assessment instruments to assess not only bias, but also the methodologic quality of the studies included. Further, this systematic review includes all the up-to-date RCTs which were not included in previous systematic reviews.

Applications

The results of this systematic review are clinically oriented and applicable in daily practices. However, facet joint interventions must be performed only after the failure of all conservative modalities of treatments.

Terminology

Facet joint pain is described variously across the globe as facet joint pain, facet joint syndrome, and zygapophysial joint pain. Similarly, the structures are also described as either facet joints or zygapophysial joints. The innervation is described as medial branches from lumbar 1 (L1) through L4, whereas L5 innervation is described as the dorsal ramus.

Peer-review

This article is concerning management of lumbar zygapophysial (facet) joint pain. This thesis is an excellent review.

REFERENCES

- 1 **Murray CJ**, Atkinson C, Bhalla K, Birbeck G, Burstein R, Chou D, Dellavalle R, Danaei G, Ezzati M, Fahimi A, Flaxman D, Foreman S, Gakidou E, Kassebaum N, Khatibzadeh S, Lim S, Lipshultz SE, London S, Lopez MF, Mokdad AH, Moran A, Moran AE, Mozaffarian D, Murphy T, Naghavi M, Pope C, Roberts T, Salomon J, Schwebel DC, Shahrzaz S, Sleet DA, Murray J, Ali MK, Atkinson C, Bartels DH, Bhalla K, Birbeck G, Burstein R, Chen H, Criqui MH, Dahodwala EL, Dorsey ER, Ebel BE, Ezzati M, Fahami S, Flaxman AD, Gonzalez-Medina D, Grant B, Hagan H, Hoffman H, Kassebaum N, Khatibzadeh S, Leasher JL, Lin J, Lipshultz SE, Lozano R, Lu Y, Mallinger L, McDermott MM, Micha R, Miller TR, Mokdad AA, Mokdad AH, Mozaffarian D, Naghavi M, Narayan KM, Omer SB, Pelizzari PM, Phillips D, Ranganathan D, Rivara FP, Roberts T, Sampson U, Sanman E, Sapkota A, Schwebel DC, Sharaz S, Shivakoti R, Singh GM, Singh D, Tavakkoli M, Towbin JA, Wilkinson JD, Zabetian A, Murray J, Ali MK, Alvarado M, Atkinson C, Baddour LM, Benjamin EJ, Bhalla K, Birbeck G, Bolliger I, Burstein R, Carnahan E, Chou D, Chugh SS, Cohen A, Colson KE, Cooper LT, Couser W, Criqui MH, Dabhadkar KC, Dellavalle RP, Jarlais D, Dorsey ER, Duber H, Ebel BE, Engell RE, Ezzati M, Felson DT, Finucane MM, Flaxman S, Flaxman AD, Fleming T, Foreman MH, Freedman G, Freeman MK, Gakidou E, Gillum RF, Gonzalez-Medina D, Gosselin R, Gutierrez HR, Hagan H, Havmoeller R, Hoffman H, Jacobsen KH, James SL, Jasrasaria R, Jayarman S, Johns N, Kassebaum N, Khatibzadeh S, Lan Q, Leasher JL, Lim S, Lipshultz SE, London S, Lopez R, Lu Y, Mallinger L, Meltzer M, Mensah GA, Michaud C, Miller TR, Mock K, Moffitt TE, Mokdad AA, Mokdad AH, Moran A, Naghavi M, Narayan KM, Nelson RG, Olives C, Omer SB, Ortblad K, Ostro B, Pelizzari PM, Phillips D, Raju M, Razavi H, Ritz B, Roberts T, Sacco RL, Salomon J, Sampson U, Schwebel DC, Shahrzaz S, Shibuya K, Silberberg D, Singh JA, Steenland K, Taylor JA, Thurston GD, Vavilala MS, Vos T, Wagner GR, Weinstock MA, Weisskopf MG, Wulf S, Murray; U.S. Burden of Disease Collaborators. The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. *JAMA* 2013; **310**: 591-608

- [PMID: 23842577 DOI: 10.1001/jama.2013.13805]
- 2 **Hoy D**, March L, Brooks P, Blyth F, Woolf A, Bain C, Williams G, Smith E, Vos T, Barendregt J, Murray C, Burstein R, Buchbinder R. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; **73**: 968-974 [PMID: 24665116 DOI: 10.1136/annrheumdis-2013-204428]
- 3 **Driscoll T**, Jacklyn G, Orchard J, Passmore E, Vos T, Freedman G, Lim S, Punnett L. The global burden of occupationally related low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014; **73**: 975-981 [PMID: 24665117 DOI: 10.1136/annrheumdis-2013-204631]
- 4 **Freburger JK**, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, Castel LD, Kalsbeek WD, Carey TS. The rising prevalence of chronic low back pain. *Arch Intern Med* 2009; **169**: 251-258 [PMID: 19204216 DOI: 10.1001/archinternmed.2008.543]
- 5 **Manchikanti L**, Singh V, Falco FJ, Benyamin RM, Hirsch JA. Epidemiology of low back pain in adults. *Neuromodulation* 2014; **17** Suppl 2: 3-10 [PMID: 25395111 DOI: 10.1111/ner.12018]
- 6 **Manchikanti L**, Pampati V, Falco FJ, Hirsch JA. An updated assessment of utilization of interventional pain management techniques in the Medicare population: 2000 - 2013. *Pain Physician* 2015; **18**: E115-E127 [PMID: 25794210]
- 7 **Rajae SS**, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: analysis of trends from 1998 to 2008. *Spine (Phila Pa 1976)* 2012; **37**: 67-76 [PMID: 21311399 DOI: 10.1097/BRS.0b013e31820cccfb]
- 8 **Dart RC**, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med* 2015; **372**: 241-248 [PMID: 25587948 DOI: 10.1056/NEJMsa1406143]
- 9 **Deyo RA**, Von Korff M, Duhkoop D. Opioids for low back pain. *BMJ* 2015; **350**: g6380 [PMID: 25561513 DOI: 10.1136/bmj.g6380]
- 10 **Manchikanti L**, Abdi S, Atluri S, Benyamin RM, Boswell MV, Buenaventura RM, Bryce DA, Burks PA, Caraway DL, Calodney AK, Cash KA, Christo PJ, Cohen SP, Colson J, Conn A, Corder H, Coubarous S, Datta S, Deer TR, Diwan S, Falco FJ, Fellows B, Geffert S, Grider JS, Gupta S, Hameed H, Hameed M, Hansen H, Helm S, Janata JW, Justiz R, Kaye AD, Lee M, Manchikanti KN, McManus CD, Onyewu O, Parr AT, Patel VB, Racz GB, Sehgal N, Sharma ML, Simopoulos TT, Singh V, Smith HS, Snook LT, Swicegood JR, Vallejo R, Ward SP, Wargo BW, Zhu J, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: guidance and recommendations. *Pain Physician* 2013; **16**: S49-283 [PMID: 23615883]
- 11 **Manchikanti L**, Atluri S, Candido KD, Boswell MV, Simopoulos TT, Grider JS, Falco FJ, Hirsch JA. Zohydro approval by food and drug administration: controversial or frightening? *Pain Physician* 2014; **17**: E437-E450 [PMID: 25054396]
- 12 **Atluri S**, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. *Pain Physician* 2014; **17**: E119-E128 [PMID: 24658483]
- 13 **Manchikanti L**, Helm Li S, Singh V, Hirsch JA. Accountable interventional pain management: a collaboration among practitioners, patients, payers, and government. *Pain Physician* 2013; **16**: E635-E670 [PMID: 24284849]
- 14 **Manchikanti L**, Pampati V, Singh V, Falco FJ. Assessment of the escalating growth of facet joint interventions in the medicare population in the United States from 2000 to 2011. *Pain Physician* 2013; **16**: E365-E378 [PMID: 23877460]
- 15 **Chou R**, Hashimoto R, Friedly J, Fu Rochelle, Dana T, Sullivan S, Bougatsos C, Jarvik J. Pain Management Injection Therapies for Low Back Pain. Technology Assessment Report ESIB0813. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. HHS 290-2012-00014-I.) Rockville, MD: Agency for Healthcare Research and Quality, 2015. Available from: URL: <http://www.cms.gov/Medicare/Coverage/DeterminationProcess/Downloads/id98TA.pdf>
- 16 **Manchikanti L**, Cash KA, Malla Y, Pampati V, Fellows B. A prospective evaluation of psychotherapeutic and illicit drug use

- in patients presenting with chronic pain at the time of initial evaluation. *Pain Physician* 2013; **16**: E1-E13 [PMID: 23340539]
- 17 **Institute of Medicine (IOM)**. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: The National Academies Press, 2011
 - 18 **Gaskin DJ**, Richard P. The economic costs of pain in the United States. *J Pain* 2012; **13**: 715-724 [PMID: 22607834 DOI: 10.1016/j.jpain.2012.03.009]
 - 19 **Martin BI**, Turner JA, Mirza SK, Lee MJ, Comstock BA, Deyo RA. Trends in health care expenditures, utilization, and health status among US adults with spine problems, 1997-2006. *Spine (Phila Pa 1976)* 2009; **34**: 2077-2084 [PMID: 19675510 DOI: 10.1097/BRS.0b013e3181b1fad1]
 - 20 **Manchikanti L**, Boswell MV, Hirsch JA. Lessons learned in the abuse of pain-relief medication: a focus on healthcare costs. *Expert Rev Neurother* 2013; **13**: 527-543; quiz 544 [PMID: 23621310 DOI: 10.1586/ern.13.33]
 - 21 **Kuslich SD**, Ulstrom CL, Michael CJ. The tissue origin of low back pain and sciatica: a report of pain response to tissue stimulation during operations on the lumbar spine using local anesthesia. *Orthop Clin North Am* 1991; **22**: 181-187 [PMID: 1826546]
 - 22 **Schwarzer AC**, Aprill CN, Derby R, Fortin J, Kine G, Bogduk N. Clinical features of patients with pain stemming from the lumbar zygapophysial joints. Is the lumbar facet syndrome a clinical entity? *Spine (Phila Pa 1976)* 1994; **19**: 1132-1137 [PMID: 8059268]
 - 23 **Manchikanti L**, Singh V, Pampati V, Damron KS, Barnhill RC, Beyer C, Cash KA. Evaluation of the relative contributions of various structures in chronic low back pain. *Pain Physician* 2001; **4**: 308-316 [PMID: 16902676]
 - 24 **DePalma MJ**, Ketchum JM, Saullo T. What is the source of chronic low back pain and does age play a role? *Pain Med* 2011; **12**: 224-233 [PMID: 21266006 DOI: 10.1111/j.1526-4637.2010.01045.x]
 - 25 **Pang WW**, Mok MS, Lin ML, Chang DP, Hwang MH. Application of spinal pain mapping in the diagnosis of low back pain--analysis of 104 cases. *Acta Anaesthesiol Sin* 1998; **36**: 71-74 [PMID: 9816715]
 - 26 **Peng BG**. Pathophysiology, diagnosis, and treatment of discogenic low back pain. *World J Orthop* 2013; **4**: 42-52 [PMID: 23610750 DOI: 10.5312/wjo.v4.i2.42]
 - 27 **Manchikanti L**, Benyamin RM, Singh V, Falco FJ, Hameed H, Derby R, Wolfert LR, Helm S, Calodney AK, Datta S, Snook LT, Caraway DL, Hirsch JA, Cohen SP. An update of the systematic appraisal of the accuracy and utility of lumbar discography in chronic low back pain. *Pain Physician* 2013; **16**: SE55-SE95 [PMID: 23615887]
 - 28 **Falco FJ**, Manchikanti L, Datta S, Sehgal N, Geffert S, Onyewu O, Singh V, Bryce DA, Benyamin RM, Simopoulos TT, Vallejo R, Gupta S, Ward SP, Hirsch JA. An update of the systematic assessment of the diagnostic accuracy of lumbar facet joint nerve blocks. *Pain Physician* 2012; **15**: E869-E907 [PMID: 23159979]
 - 29 **Bogduk N**. Low back pain. Clinical Anatomy of Lumbar Spine and Sacrum, 4th edition. New York: Churchill Livingstone, 2005: 183-216
 - 30 **Manchikanti L**, Hirsch JA. Clinical management of radicular pain. *Expert Rev Neurother* 2015; **15**: 681-693 [PMID: 25982996 DOI: 10.1586/14737175.2015.1048226]
 - 31 **Datta S**, Manchikanti L, Falco FJ, Calodney AK, Atluri S, Benyamin RM, Buenaventura RM, Cohen SP. Diagnostic utility of selective nerve root blocks in the diagnosis of lumbosacral radicular pain: systematic review and update of current evidence. *Pain Physician* 2013; **16**: SE97-S124 [PMID: 23615888]
 - 32 **Rubinstein SM**, van Tulder M. A best-evidence review of diagnostic procedures for neck and low-back pain. *Best Pract Res Clin Rheumatol* 2008; **22**: 471-482 [PMID: 18519100 DOI: 10.1016/j.berh.2007.12.003]
 - 33 **Markwalder TM**, Mérat M. The lumbar and lumbosacral facet-syndrome. Diagnostic measures, surgical treatment and results in 119 patients. *Acta Neurochir (Wien)* 1994; **128**: 40-46 [PMID: 7847142]
 - 34 **Tessitore E**, Molliqaj G, Schatlo B, Schaller K. Clinical evaluation and surgical decision making for patients with lumbar discogenic pain and facet syndrome. *Eur J Radiol* 2015; **84**: 765-770 [PMID: 24801263 DOI: 10.1016/j.ejrad.2014.03.016]
 - 35 **Bogduk N**. On diagnostic blocks for lumbar zygapophysial joint pain. *F1000 Med Rep* 2010; **2**: 57 [PMID: 21173871 DOI: 10.3410/M2-57]
 - 36 **Cavanaugh JM**, Lu Y, Chen C, Kallakuri S. Pain generation in lumbar and cervical facet joints. *J Bone Joint Surg Am* 2006; **88 Suppl 2**: 63-67 [PMID: 16595446]
 - 37 **Bogduk N**, Wilson AS, Tynan W. The human lumbar dorsal rami. *J Anat* 1982; **134**: 383-397 [PMID: 7076562]
 - 38 **Ishikawa T**, Miyagi M, Ohtori S, Aoki Y, Ozawa T, Doya H, Saito T, Moriya H, Takahashi K. Characteristics of sensory DRG neurons innervating the lumbar facet joints in rats. *Eur Spine J* 2005; **14**: 559-564 [PMID: 15690212]
 - 39 **Henry JL**, Yashpal K, Vernon H, Kim J, Im HJ. Lumbar facet joint compressive injury induces lasting changes in local structure, nociceptive scores, and inflammatory mediators in a novel rat model. *Pain Res Treat* 2012; **2012**: 127636 [PMID: 22966427 DOI: 10.1155/2012/127636]
 - 40 **Kras JV**, Dong L, Winkelstein BA. Increased interleukin-1 α and prostaglandin E2 expression in the spinal cord at 1 day after painful facet joint injury: evidence of early spinal inflammation. *Spine (Phila Pa 1976)* 2014; **39**: 207-212 [PMID: 24253784 DOI: 10.1097/BRS.0000000000000107]
 - 41 **Sagar DR**, Ashraf S, Xu L, Burston JJ, Menhinick MR, Poulter CL, Bennett AJ, Walsh DA, Chapman V. Osteoprotegerin reduces the development of pain behaviour and joint pathology in a model of osteoarthritis. *Ann Rheum Dis* 2014; **73**: 1558-1565 [PMID: 23723320 DOI: 10.1136/annrheumdis-2013-203260]
 - 42 **Bullock CM**, Wookey P, Bennett A, Mobasher A, Dickerson I, Kelly S. Peripheral calcitonin gene-related peptide receptor activation and mechanical sensitization of the joint in rat models of osteoarthritis pain. *Arthritis Rheumatol* 2014; **66**: 2188-2200 [PMID: 24719311 DOI: 10.1002/art.38656]
 - 43 **Quinn KP**, Dong L, Golder FJ, Winkelstein BA. Neuronal hyperexcitability in the dorsal horn after painful facet joint injury. *Pain* 2010; **151**: 414-421 [PMID: 20739124 DOI: 10.1016/j.pain.2010.07.034]
 - 44 **Dong L**, Odeleye AO, Jordan-Sciutto KL, Winkelstein BA. Painful facet joint injury induces neuronal stress activation in the DRG: implications for cellular mechanisms of pain. *Neurosci Lett* 2008; **443**: 90-94 [PMID: 18675314 DOI: 10.1016/j.neulet.2008.07.059]
 - 45 **Sakuma Y**, Ohtori S, Miyagi M, Ishikawa T, Inoue G, Doya H, Koshi T, Ito T, Yamashita M, Yamauchi K, Suzuki M, Moriya H, Takahashi K. Up-regulation of p55 TNF alpha-receptor in dorsal root ganglia neurons following lumbar facet joint injury in rats. *Eur Spine J* 2007; **16**: 1273-1278 [PMID: 17468886]
 - 46 **Gellhorn AC**, Katz JN, Suri P. Osteoarthritis of the spine: the facet joints. *Nat Rev Rheumatol* 2013; **9**: 216-224 [PMID: 23147891 DOI: 10.1038/nrrheum.2012.199]
 - 47 **Kalichman L**, Li L, Kim DH, Guermazi A, Berkin V, O'Donnell CJ, Hoffmann U, Cole R, Hunter DJ. Facet joint osteoarthritis and low back pain in the community-based population. *Spine (Phila Pa 1976)* 2008; **33**: 2560-2565 [PMID: 18923337 DOI: 10.1097/BRS.0b013e318184ef95]
 - 48 **Eubanks JD**, Lee MJ, Cassinelli E, Ahn NU. Prevalence of lumbar facet arthrosis and its relationship to age, sex, and race: an anatomic study of cadaveric specimens. *Spine (Phila Pa 1976)* 2007; **32**: 2058-2062 [PMID: 17762805]
 - 49 **HARRIS RI**, MACNAB I. Structural changes in the lumbar intervertebral discs; their relationship to low back pain and sciatica. *J Bone Joint Surg Br* 1954; **36-B**: 304-322 [PMID: 13163117]
 - 50 **Chou R**, Huffman L. Guideline for the Evaluation and Management of Low Back Pain: Evidence Review. Glenview, IL: American Pain Society, 2009

- 51 **Manchikanti L**, Datta S, Derby R, Wolfer LR, Benyamin RM, Hirsch JA. A critical review of the American Pain Society clinical practice guidelines for interventional techniques: part I. Diagnostic interventions. *Pain Physician* 2010; **13**: E141-E174 [PMID: 20495596]
- 52 **Carragee EJ**, Haldeman S, Hurwitz E. The pyrite standard: the Midas touch in the diagnosis of axial pain syndromes. *Spine J* 2007; **7**: 27-31 [PMID: 17197329]
- 53 **Hancock MJ**, Maher CG, Latimer J, Spindler MF, McAuley JH, Laslett M, Bogduk N. Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *Eur Spine J* 2007; **16**: 1539-1550 [PMID: 17566796]
- 54 **Falco FJ**, Manchikanti L, Datta S, Sehgal N, Geffert S, Onyewu O, Zhu J, Coubarous S, Hameed M, Ward SP, Sharma M, Hameed H, Singh V, Boswell MV. An update of the effectiveness of therapeutic lumbar facet joint interventions. *Pain Physician* 2012; **15**: E909-E953 [PMID: 23159980]
- 55 **Manchikanti L**, Datta S, Gupta S, Munglani R, Bryce DA, Ward SP, Benyamin RM, Sharma ML, Helm S, Fellows B, Hirsch JA. A critical review of the American Pain Society clinical practice guidelines for interventional techniques: part 2. Therapeutic interventions. *Pain Physician* 2010; **13**: E215-E264 [PMID: 20648212]
- 56 **van Middelkoop M**, Rubinstein SM, Kuijpers T, Verhagen AP, Ostelo R, Koes BW, van Tulder MW. A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J* 2011; **20**: 19-39 [PMID: 20640863 DOI: 10.1007/s00586-010-1518-3]
- 57 **Furlan AD**, Yazdi F, Tsertsvadze A, Gross A, Van Tulder M, Santaguida L, Cherkin D, Gagnier J, Ammendolia C, Ansari MT, Ostermann T, Dryden T, Doucette S, Skidmore B, Daniel R, Tsouros S, Weeks L, Galipeau J. Complementary and alternative therapies for back pain II. *Evid Rep Technol Assess (Full Rep)* 2010; **(194)**: 1-764 [PMID: 23126534]
- 58 **Chung JW**, Zeng Y, Wong TK. Drug therapy for the treatment of chronic nonspecific low back pain: systematic review and meta-analysis. *Pain Physician* 2013; **16**: E685-E704 [PMID: 24284847]
- 59 **Deyo RA**. Fusion surgery for lumbar degenerative disc disease: still more questions than answers. *Spine J* 2015; **15**: 272-274 [PMID: 25598279 DOI: 10.1016/j.spinee.2014.11.004]
- 60 **Chaparro LE**, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared with placebo or other treatments for chronic low back pain: an update of the Cochrane Review. *Spine (Phila Pa 1976)* 2014; **39**: 556-563 [PMID: 24480962 DOI: 10.1097/BRS.0000000000000249]
- 61 **Leite VF**, Buehler AM, El Abd O, Benyamin RM, Pimentel DC, Chen J, Hsing WT, Mazloomdoost D, Amadera JE. Anti-nerve growth factor in the treatment of low back pain and radiculopathy: a systematic review and a meta-analysis. *Pain Physician* 2014; **17**: E45-E60 [PMID: 24452657]
- 62 **Pimentel DC**, El Abd O, Benyamin RM, Buehler AM, Leite VF, Mazloomdoost D, Chen J, Hsing WT, Amadera JE. Anti-tumor necrosis factor antagonists in the treatment of low back pain and radiculopathy: a systematic review and meta-analysis. *Pain Physician* 2014; **17**: E27-E44 [PMID: 24452656]
- 63 **Kuijpers T**, van Middelkoop M, Rubinstein SM, Ostelo R, Verhagen A, Koes BW, van Tulder MW. A systematic review on the effectiveness of pharmacological interventions for chronic non-specific low-back pain. *Eur Spine J* 2011; **20**: 40-50 [PMID: 20680369 DOI: 10.1007/s00586-010-1541-4]
- 64 **White AP**, Arnold PM, Norvell DC, Ecker E, Fehlings MG. Pharmacologic management of chronic low back pain: synthesis of the evidence. *Spine (Phila Pa 1976)* 2011; **36**: S131-S143 [PMID: 21952185 DOI: 10.1097/BRS.0b013e31822f178f]
- 65 **Chou R**, Huffman LH. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med* 2007; **147**: 505-514 [PMID: 17909211]
- 66 **Leavitt SB**. NSAID dangers may limit pain-relief options. *Pain-Topics News/Research*. [Updated 2010 Mar 14]. Available from: URL: <http://updates.pain-topics.org/2010/03/nsaid-dangers-may-limit-pain-relief.html>
- 67 **Moore A**, Wiffen P, Kalso E. Antiepileptic drugs for neuropathic pain and fibromyalgia. *JAMA* 2014; **312**: 182-183 [PMID: 25005656 DOI: 10.1001/jama.2014.6336]
- 68 **Manchikanti L**, Falco FJ, Benyamin RM, Helm S, Singh V, Hirsch JA. Value-based interventional pain management: a review of medicare national and local coverage determination policies. *Pain Physician* 2013; **16**: E145-E180 [PMID: 23703416]
- 69 **Leggett LE**, Soril LJ, Lorenzetti DL, Noseworthy T, Steadman R, Tiwana S, Clement F. Radiofrequency ablation for chronic low back pain: a systematic review of randomized controlled trials. *Pain Res Manag* 2014; **19**: e146-e153 [PMID: 25068973]
- 70 **Poetscher AW**, Gentil AF, Lenza M, Ferretti M. Radiofrequency denervation for facet joint low back pain: a systematic review. *Spine (Phila Pa 1976)* 2014; **39**: E842-E849 [PMID: 24732848 DOI: 10.1097/BRS.0000000000000337]
- 71 **Bogduk N**, Dreyfuss P, Govind J. A narrative review of lumbar medial branch neurotomy for the treatment of back pain. *Pain Med* 2009; **10**: 1035-1045 [PMID: 19694977 DOI: 10.1111/j.1526-4637.2009.00692.x]
- 72 **Bogduk N**. A narrative review of intraarticular corticosteroid injections for low back pain. *Pain Med* 2005; **6**: 287-296 [DOI: 10.1111/j.1526-4637.2005.00048.x]
- 73 **Niemisto L**, Kalso E, Malmivaara A, Seitsalo S, Hurri H. Radiofrequency denervation for neck and back pain. A systematic review of randomized controlled trials. *Cochrane Database Syst Rev* 2003; **(1)**: CD004058 [PMID: 12535508]
- 74 **Cohen SP**, Huang JH, Brummett C. Facet joint pain--advances in patient selection and treatment. *Nat Rev Rheumatol* 2013; **9**: 101-116 [PMID: 23165358 DOI: 10.1038/nrrheum.2012.198]
- 75 **Manchikanti L**, Staats PS, Nampiaparampil DE, Hirsch JA. What is the Role of Epidural Injections in the Treatment of Lumbar Discogenic Pain: A Systematic Review of Comparative Analysis with Fusion. *Korean J Pain* 2015; **28**: 75-87 [PMID: 25852828 DOI: 10.3344/kjp.2015.28.2.75]
- 76 **Manchikanti L**, Falco FJ, Singh V, Benyamin RM, Racz GB, Helm S, Caraway DL, Calodney AK, Snook LT, Smith HS, Gupta S, Ward SP, Grider JS, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part I: introduction and general considerations. *Pain Physician* 2013; **16**: S1-48 [PMID: 23615882]
- 77 **Liberati A**, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009; **151**: W65-W94 [PMID: 19622512]
- 78 **Furlan AD**, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; **34**: 1929-1941 [PMID: 19680101 DOI: 10.1097/BRS.0b013e3181b1c99f]
- 79 **Manchikanti L**, Hirsch JA, Cohen SP, Heavner JE, Falco FJ, Diwan S, Boswell MV, Candido KD, Onyewu CO, Zhu J, Sehgal N, Kaye AD, Benyamin RM, Helm S, Singh V, Datta S, Abdi S, Christo PJ, Hameed H, Hameed M, Vallejo R, Pampati V, Racz GB, Raj PP. Assessment of methodologic quality of randomized trials of interventional techniques: development of an interventional pain management specific instrument. *Pain Physician* 2014; **17**: E263-E290 [PMID: 24850111]
- 80 **Lucas NP**, Macaskill P, Irwig L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). *J Clin Epidemiol* 2010; **63**: 854-861 [PMID: 20056381 DOI: 10.1016/j.jclinepi.2009]
- 81 **Manchikanti L**, Hirsch JA, Heavner JE, Cohen SP, Benyamin RM, Sehgal N, Falco FJ, Vallejo R, Onyewu O, Zhu J, Kaye AD, Boswell MV, Helm S, Candido KD, Diwan S, Simopoulos TT, Singh V, Pampati V, Racz GB, Raj PP. Development of an interventional pain management specific instrument for methodologic quality

- assessment of nonrandomized studies of interventional techniques. *Pain Physician* 2014; **17**: E291-E317 [PMID: 24850112]
- 82 **Manchikanti L**, Falco FJ, Benyamin RM, Kaye AD, Boswell MV, Hirsch JA. A modified approach to grading of evidence. *Pain Physician* 2014; **17**: E319-E325 [PMID: 24850113]
- 83 **Staal JB**, de Bie RA, de Vet HC, Hildebrandt J, Nelemans P. Injection therapy for subacute and chronic low back pain: an updated Cochrane review. *Spine (Phila Pa 1976)* 2009; **34**: 49-59 [PMID: 19127161 DOI: 10.1097/BRS.0b013e3181909558]
- 84 **Schwarzer AC**, Wang SC, Bogduk N, McNaught PJ, Laurent R. Prevalence and clinical features of lumbar zygapophysial joint pain: a study in an Australian population with chronic low back pain. *Ann Rheum Dis* 1995; **54**: 100-106 [PMID: 7702395]
- 85 **Manchikanti L**, Pampati V, Fellows B, Baha AG. The inability of the clinical picture to characterize pain from facet joints. *Pain Physician* 2000; **3**: 158-166 [PMID: 16906195]
- 86 **Manchikanti L**, Pampati V, Fellows B, Bakht CE. Prevalence of lumbar facet joint pain in chronic low back pain. *Pain Physician* 1999; **2**: 59-64 [PMID: 16906217]
- 87 **Manchikanti L**, Pampati V, Fellows B, Bakht CE. The diagnostic validity and therapeutic value of lumbar facet joint nerve blocks with or without adjuvant agents. *Curr Rev Pain* 2000; **4**: 337-344 [PMID: 10998741]
- 88 **Manchikanti L**, Hirsch JA, Pampati V. Chronic low back pain of facet (zygapophysial) joint origin: is there a difference based on involvement of single or multiple spinal regions? *Pain Physician* 2003; **6**: 399-405 [PMID: 16871288]
- 89 **Manchikanti L**, Singh V, Pampati V, Damron KS, Beyer CD, Barnhill RC. Is there correlation of facet joint pain in lumbar and cervical spine? An evaluation of prevalence in combined chronic low back and neck pain. *Pain Physician* 2002; **5**: 365-371 [PMID: 16886014]
- 90 **Manchikanti L**, Boswell MV, Singh V, Pampati V, Damron KS, Beyer CD. Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. *BMC Musculoskelet Disord* 2004; **5**: 15 [PMID: 15169547 DOI: 10.1186/1471-2474-5-15]
- 91 **Manchukonda R**, Manchikanti KN, Cash KA, Pampati V, Manchikanti L. Facet joint pain in chronic spinal pain: an evaluation of prevalence and false-positive rate of diagnostic blocks. *J Spinal Disord Tech* 2007; **20**: 539-545 [PMID: 17912133]
- 92 **Manchikanti L**, Manchukonda R, Pampati V, Damron KS, McManus CD. Prevalence of facet joint pain in chronic low back pain in postsurgical patients by controlled comparative local anesthetic blocks. *Arch Phys Med Rehabil* 2007; **88**: 449-455 [PMID: 17398245]
- 93 **Manchikanti L**, Pampati V, Rivera J, Fellows B, Beyer C, Damron K. Role of facet joints in chronic low back pain in the elderly: a controlled comparative prevalence study. *Pain Pract* 2001; **1**: 332-337 [PMID: 17147574]
- 94 **Manchikanti L**, Pampati V, Singh V, Beyer C, Damron K, Fellows B. Evaluation of the role of facet joints in persistent low back pain in obesity: a controlled, prospective, comparative evaluation. *Pain Physician* 2001; **4**: 266-272 [PMID: 16900253]
- 95 **Manchikanti L**, Pampati S, Cash KA. Making sense of the accuracy of diagnostic lumbar facet joint nerve blocks: an assessment of the implications of 50% relief, 80% relief, single block, or controlled diagnostic blocks. *Pain Physician* 2010; **13**: 133-143 [PMID: 20309379]
- 96 **Tekin I**, Mirzai H, Ok G, Erbuyun K, Vatansever D. A comparison of conventional and pulsed radiofrequency denervation in the treatment of chronic facet joint pain. *Clin J Pain* 2007; **23**: 524-529 [PMID: 17575493]
- 97 **van Wijk RM**, Geurts JW, Wynne HJ, Hammink E, Buskens E, Lousberg R, Knape JT, Groen GJ. Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain: a randomized, double-blind, sham lesion-controlled trial. *Clin J Pain* 2005; **21**: 335-344 [PMID: 15951652]
- 98 **Dobrogowski J**, Wrzosek A, Wordliczek J. Radiofrequency denervation with or without addition of pentoxifylline or methylprednisolone for chronic lumbar zygapophysial joint pain. *Pharmacol Rep* 2005; **57**: 475-480 [PMID: 16129914]
- 99 **van Kleef M**, Barendse GA, Kessels A, Voets HM, Weber WE, de Lange S. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. *Spine (Phila Pa 1976)* 1999; **24**: 1937-1942 [PMID: 10515020]
- 100 **Moon JY**, Lee PB, Kim YC, Choi SP, Sim WS. An alternative distal approach for the lumbar medial branch radiofrequency denervation: a prospective randomized comparative study. *Anesth Analg* 2013; **116**: 1133-1140 [PMID: 23558841 DOI: 10.1213/ANE.0b013e31828b35fe]
- 101 **Lakemeier S**, Lind M, Schultz W, Fuchs-Winkelmann S, Timmesfeld N, Foelsch C, Peterlein CD. A comparison of intraarticular lumbar facet joint steroid injections and lumbar facet joint radiofrequency denervation in the treatment of low back pain: a randomized, controlled, double-blind trial. *Anesth Analg* 2013; **117**: 228-235 [PMID: 23632051 DOI: 10.1213/ANE.0b013e3182910c4d]
- 102 **Manchikanti L**, Singh V, Falco FJ, Cash KA, Pampati V. Evaluation of lumbar facet joint nerve blocks in managing chronic low back pain: a randomized, double-blind, controlled trial with a 2-year follow-up. *Int J Med Sci* 2010; **7**: 124-135 [PMID: 20567613]
- 103 **Carette S**, Marcoux S, Truchon R, Grondin C, Gagnon J, Allard Y, Latulippe M. A controlled trial of corticosteroid injections into facet joints for chronic low back pain. *N Engl J Med* 1991; **325**: 1002-1007 [PMID: 1832209]
- 104 **Fuchs S**, Erbe T, Fischer HL, Tibesku CO. Intraarticular hyaluronic acid versus glucocorticoid injections for nonradicular pain in the lumbar spine. *J Vasc Interv Radiol* 2005; **16**: 1493-1498 [PMID: 16319156]
- 105 **Nath S**, Nath CA, Pettersson K. Percutaneous lumbar zygapophysial (Facet) joint neurotomy using radiofrequency current, in the management of chronic low back pain: a randomized double-blind trial. *Spine (Phila Pa 1976)* 2008; **33**: 1291-1297; discussion 1298 [PMID: 18496338 DOI: 10.1097/BRS.0b013e31817329f0]
- 106 **Yun DH**, Kim HS, Yoo SD, Kim DH, Chon JM, Choi SH, Hwang DG, Jung PK. Efficacy of ultrasonography-guided injections in patients with facet syndrome of the low lumbar spine. *Ann Rehabil Med* 2012; **36**: 66-71 [PMID: 22506237 DOI: 10.5535/arm.2012.36.1.66]
- 107 **Ribeiro LH**, Furtado RN, Konai MS, Andreo AB, Rosenfeld A, Natour J. Effect of facet joint injection versus systemic steroids in low back pain: a randomized controlled trial. *Spine (Phila Pa 1976)* 2013; **38**: 1995-2002 [PMID: 23921331 DOI: 10.1097/BRS.0b013e3182a76df1]
- 108 **Civelek E**, Cansever T, Kabatas S, Kircelli A, Yilmaz C, Musluman M, Ofluoglu D, Caner H. Comparison of effectiveness of facet joint injection and radiofrequency denervation in chronic low back pain. *Turk Neurosurg* 2012; **22**: 200-206 [PMID: 22437295 DOI: 10.5137/1019-5149.JTN.5207-11.1]
- 109 **Cohen SP**, Williams KA, Kurihara C, Nguyen C, Shields C, Kim P, Griffith SR, Larkin TM, Crooks M, Williams N, Morlando B, Strassels SA. Multicenter, randomized, comparative cost-effectiveness study comparing 0, 1, and 2 diagnostic medial branch (facet joint nerve) block treatment paradigms before lumbar facet radiofrequency denervation. *Anesthesiology* 2010; **113**: 395-405 [PMID: 20613471 DOI: 10.1097/ALN.0b013e3181e33ae5]
- 110 **Leclaire R**, Fortin L, Lambert R, Bergeron YM, Rossignol M. Radiofrequency facet joint denervation in the treatment of low back pain: a placebo-controlled clinical trial to assess efficacy. *Spine (Phila Pa 1976)* 2001; **26**: 1411-1416; discussion 1417 [PMID: 11458140]
- 111 **Gauci C**. Radiofrequency neurotomy for chronic lumbar facet pain--interpreting the evidence. *Pain Pract* 2010; **10**: 261; author reply 261-262 [PMID: 20546520 DOI: 10.1111/j.1533-2500.2010.00369_1.x]
- 112 **Schwarzer AC**, Wang SC, O'Driscoll D, Harrington T, Bogduk N, Laurent R. The ability of computed tomography to identify a painful zygapophysial joint in patients with chronic low back pain.

- Spine* (Phila Pa 1976) 1995; **20**: 907-912 [PMID: 7644955]
- 113 **Laslett M**, McDonald B, Aprill CN, Tropp H, Oberg B. Clinical predictors of screening lumbar zygapophyseal joint blocks: development of clinical prediction rules. *Spine J* 2006; **6**: 370-379 [PMID: 16825041]
 - 114 **Revel ME**, Listrat VM, Chevalier XJ, Dougados M, N'guyen MP, Vallee C, Wybier M, Gires F, Amor B. Facet joint block for low back pain: identifying predictors of a good response. *Arch Phys Med Rehabil* 1992; **73**: 824-828 [PMID: 1387521]
 - 115 **Revel M**, Poiraudau S, Auleley GR, Payan C, Denke A, Nguyen M, Chevrot A, Fermanian J. Capacity of the clinical picture to characterize low back pain relieved by facet joint anesthesia. Proposed criteria to identify patients with painful facet joints. *Spine* (Phila Pa 1976) 1998; **23**: 1972-1976; discussion 1977 [PMID: 9779530]
 - 116 **Young S**, Aprill C, Laslett M. Correlation of clinical examination characteristics with three sources of chronic low back pain. *Spine J* 2003; **3**: 460-465 [PMID: 14609690]
 - 117 **Manchikanti L**, Manchikanti KN, Cash KA, Singh V, Giordano J. Age-related prevalence of facet-joint involvement in chronic neck and low back pain. *Pain Physician* 2008; **11**: 67-75 [PMID: 18196171]
 - 118 **DePalma MJ**, Ketchum JM, Saullo TR. Etiology of chronic low back pain in patients having undergone lumbar fusion. *Pain Med* 2011; **12**: 732-739 [PMID: 21481166 DOI: 10.1111/j.1526-4637.2011.01098.x]
 - 119 **DePalma MJ**, Ketchum JM, Trussell BS, Saullo TR, Slipman CW. Does the location of low back pain predict its source? *PMR* 2011; **3**: 33-39 [PMID: 21257131 DOI: 10.1016/j.pmrj.2010.09.006]
 - 120 **DePalma M**, Ketchum J, Saullo T, Schofferman J. Structural etiology of chronic low back pain due to motor vehicle collision. *Pain Med* 2011; **12**: 1622-1627 [PMID: 21958329 DOI: 10.1111/j.1526-4637.2011.01246.x]
 - 121 **Manchikanti L**, Cash KA, Pampati V, Fellows B. Influence of psychological variables on the diagnosis of facet joint involvement in chronic spinal pain. *Pain Physician* 2008; **11**: 145-160 [PMID: 18354709]
 - 122 **Manchikanti L**, Damron KS, Rivera JJ, McManus CD, Jackson SD, Barnhill RC, Martin JC. Evaluation of the effect of sedation as a confounding factor in the diagnostic validity of lumbar facet joint pain: a prospective, randomized, double-blind, placebo-controlled evaluation. *Pain Physician* 2004; **7**: 411-417 [PMID: 16858481]
 - 123 **Manchikanti L**, Pampati V, Damron K. The role of placebo and nocebo effects of perioperative administration of sedatives and opioids in interventional pain management. *Pain Physician* 2005; **8**: 349-355 [PMID: 16850057]
 - 124 **Petersen GL**, Finnerup NB, Colloca L, Amanzio M, Price DD, Jensen TS, Vase L. The magnitude of nocebo effects in pain: a meta-analysis. *Pain* 2014; **155**: 1426-1434 [PMID: 24780622 DOI: 10.1016/j.pain.2014.04.016]
 - 125 **Quill TE**, Holloway RG. Evidence, preferences, recommendations-finding the right balance in patient care. *N Engl J Med* 2012; **366**: 1653-1655 [PMID: 22551123 DOI: 10.1056/NEJMp1201535]
 - 126 **Manchikanti L**, Giordano J, Fellows B, Hirsch JA. Placebo and nocebo in interventional pain management: a friend or a foe--or simply foes? *Pain Physician* 2011; **14**: E157-E175 [PMID: 21412379]
 - 127 **US Department of Health and Human Services**. Office of Inspector General (OIG). Medicare Payments for Facet Joint Injection Services (OEI-05-07-00200). [Updated 2008 Sept]. Available from: URL: <http://www.oig.hhs.gov/oei/reports/oei-05-07-00200.pdf>
 - 128 **Chou R**, Atlas SJ, Loeser JD, Rosenquist RW, Stanos SP. Guideline warfare over interventional therapies for low back pain: can we raise the level of discourse? *J Pain* 2011; **12**: 833-839 [PMID: 21742563 DOI: 10.1016/j.jpain.2011.04.012]
 - 129 **Manchikanti L**, Benyamin RM, Falco FJ, Caraway DL, Datta S, Hirsch JA. Guidelines warfare over interventional techniques: is there a lack of discourse or straw man? *Pain Physician* 2012; **15**: E1-E26 [PMID: 22270745]
 - 130 **Häuser W**, Bartram C, Bartram-Wunn E, Tölle T. Adverse events attributable to nocebo in randomized controlled drug trials in fibromyalgia syndrome and painful diabetic peripheral neuropathy: systematic review. *Clin J Pain* 2012; **28**: 437-451 [PMID: 22336767 DOI: 10.1097/AJP.0b013e3182321ad8]
 - 131 **Howick J**, Friedemann C, Tsakok M, Watson R, Tsakok T, Thomas J, Perera R, Fleming S, Heneghan C. Are treatments more effective than placebos? A systematic review and meta-analysis. *PLoS One* 2013; **8**: e62599 [PMID: 23690944 DOI: 10.1371/journal.pone.0062599]
 - 132 **Hróbjartsson A**, Gøtzsche PC. Placebo interventions for all clinical conditions. *Cochrane Database Syst Rev* 2010; **(1)**: CD003974 [PMID: 20091554 DOI: 10.1002/14651858.CD003974.pub3]
 - 133 **Lyby PS**, Forsberg JT, Asli O, Flaten MA. Induced fear reduces the effectiveness of a placebo intervention on pain. *Pain* 2012; **153**: 1114-1121 [PMID: 22464696 DOI: 10.1016/j.pain.2012.02.042]
 - 134 **Gerdesmeyer L**, Wagenpfeil S, Birkenmaier C, Veihelmann A, Hauschild M, Wagner K, Muderis MA, Gollwitzer H, Diehl P, Toepfer A. Percutaneous epidural lysis of adhesions in chronic lumbar radicular pain: a randomized, double-blind, placebo-controlled trial. *Pain Physician* 2013; **16**: 185-196 [PMID: 23703406]
 - 135 **Ghahreman A**, Ferch R, Bogduk N. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. *Pain Med* 2010; **11**: 1149-1168 [PMID: 20704666 DOI: 10.1111/j.1526-4637.2010.00908.x]
 - 136 **Manchikanti L**, Nampiaparampil DE, Manchikanti KN, Falco FJ, Singh V, Benyamin RM, Kaye AD, Sehgal N, Soin A, Simopoulos TT, Bakshi S, Gharibo CG, Gilligan CJ, Hirsch JA. Comparison of the efficacy of saline, local anesthetics, and steroids in epidural and facet joint injections for the management of spinal pain: A systematic review of randomized controlled trials. *Surg Neurol Int* 2015; **6**: S194-S235 [PMID: 26005584 DOI: 10.4103/2152-7806.156598]
 - 137 **Manchikanti L**, Benyamin RM, Falco FJ, Kaye AD, Hirsch JA. Do Epidural Injections Provide Short- and Long-term Relief for Lumbar Disc Herniation? A Systematic Review. *Clin Orthop Relat Res* 2015; **473**: 1940-1956 [PMID: 24515404 DOI: 10.1007/s11999-014-3490-4]
 - 138 **Manchikanti L**, Nampiaparampil DE, Candido KD, Bakshi S, Grider JS, Falco FJ, Sehgal N, Hirsch JA. Do cervical epidural injections provide long-term relief in neck and upper extremity pain? A systematic review. *Pain Physician* 2015; **18**: 39-60 [PMID: 25675059]
 - 139 **Manchikanti L**, Kaye AD, Manchikanti K, Boswell M, Pampati V, Hirsch J. Efficacy of epidural injections in the treatment of lumbar central spinal stenosis: a systematic review. *Anesth Pain Med* 2015; **5**: e23139 [PMID: 25789241 DOI: 10.5812/aapm.23139]
 - 140 **Friedly JL**, Comstock BA, Turner JA, Heagerty PJ, Deyo RA, Sullivan SD, Bauer Z, Bresnahan BW, Avins AL, Nedeljkovic SS, Nerenz DR, Standaert C, Kessler L, Akuthota V, Annaswamy T, Chen A, Diehn F, Firtch W, Gerges FJ, Gilligan C, Goldberg H, Kennedy DJ, Mandel S, Tyburski M, Sanders W, Sibell D, Smuck M, Wasan A, Won L, Jarvik JG. A randomized trial of epidural glucocorticoid injections for spinal stenosis. *N Engl J Med* 2014; **371**: 11-21 [PMID: 24988555 DOI: 10.1056/NEJMoa1313265]
 - 141 **Manchikanti L**, Candido KD, Kaye AD, Boswell MV, Benyamin RM, Falco FJ, Gharibo CG, Hirsch JA. Randomized trial of epidural injections for spinal stenosis published in the New England Journal of Medicine: further confusion without clarification. *Pain Physician* 2014; **17**: E475-E488 [PMID: 25054398]
 - 142 **Cohen SP**, Hayek S, Semenov Y, Pasquina PF, White RL, Veizi E, Huang JH, Kurihara C, Zhao Z, Guthmiller KB, Griffith SR, Verdun AV, Giampetro DM, Vorobeychik Y. Epidural steroid injections, conservative treatment, or combination treatment for cervical radicular pain: a multicenter, randomized, comparative-effectiveness study. *Anesthesiology* 2014; **121**: 1045-1055 [PMID: 25335172 DOI: 10.1097/ALN.0000000000000409]
 - 143 **Cohen SP**, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Epidural steroids: a comprehensive, evidence-based review. *Reg*

Anesth Pain Med 2013; **38**: 175-200 [PMID: 23598728 DOI: 10.1097/AAP.0b013e31828ea086]

144 **MacVicar J**, Borowczyk JM, MacVicar AM, Loughnan BM,

Bogduk N. Lumbar medial branch radiofrequency neurotomy in New Zealand. *Pain Med* 2013; **14**: 639-645 [PMID: 23279154 DOI: 10.1111/pme.12000]

P- Reviewer: Chen C, Guerado E, Korovessis P, Tokuhashi Y

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Liu SQ



Methicillin-resistant *Staphylococcus aureus* infected gluteal compartment syndrome with rhabdomyolysis in a bodybuilder

Colin YL Woon, Kushal R Patel, Benjamin A Goldberg

Colin YL Woon, Kushal R Patel, Benjamin A Goldberg, Department of Orthopaedic Surgery, University of Illinois at Chicago, Chicago, IL 60612, United States

Author contributions: Woon CYL designed the report and wrote the paper; Patel KR collected data and revised the paper; Goldberg BA revised and reviewed the paper for critical content.

Institutional review board statement: None.

Informed consent statement: The involved subject provided written informed consent for the study.

Conflict-of-interest statement: The authors declare no conflicts of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Colin YL Woon, MD, Department of Orthopaedic Surgery, University of Illinois at Chicago, 835 S. Wolcott Avenue, M/C 844, Chicago, IL 60612, United States. wolv23@gmail.com
Telephone: +1-312-9969858
Fax: +1-312-9969025

Received: February 3, 2016

Peer-review started: February 14, 2016

First decision: March 1, 2016

Revised: March 10, 2016

Accepted: March 24, 2016

Article in press: March 25, 2016

Published online: May 18, 2016

Abstract

Gluteal compartment syndrome (GCS) is a rare condition. We present a case of gluteal muscle strain with hematoma formation, methicillin-resistant *Staphylococcus aureus* (MRSA) superinfection, leading to acute GCS, rhabdomyolysis and acute kidney injury. This combination of diagnoses has not been reported in the literature. A 36-year-old Caucasian male presented with buttock pain, swelling and fever after lifting weights. Gluteal compartment pressure was markedly elevated compared with the contralateral side. Investigations revealed elevated white blood cell, erythrocyte sedimentation rate, C-reactive protein, creatine kinase, creatinine and lactic acid. Urinalysis was consistent with myoglobinuria. Magnetic resonance imaging showed increased T2 signal in the gluteus maximus and a central hematoma. Cultures taken from the emergency debridement and fasciotomy revealed MRSA. He had repeat, debridement 2 d later, and delayed primary closure 3 d after. GCS is rare and must be suspected when patients present with pain and swelling after an inciting event. They are easily diagnosed with compartment pressure monitoring. The treatment of gluteal abscess and compartment syndrome is the same and involves rapid surgical debridement.

Key words: Compartment syndrome; Rhabdomyolysis; Methicillin-resistant *Staphylococcus aureus*; Gluteal compartment; Acute kidney injury

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Gluteal compartment syndrome (GCS) is rare. Methicillin-resistant *Staphylococcus aureus* infected GCS with rhabdomyolysis and acute kidney injury has

not been reported. Compartment pressure monitoring and magnetic resonance imaging are useful for the diagnosis of this condition. Successful management comprises surgical fasciotomy, debridement together with antibiotics.

Woon CYL, Patel KR, Goldberg BA. Methicillin-resistant *Staphylococcus aureus* infected gluteal compartment syndrome with rhabdomyolysis in a bodybuilder. *World J Orthop* 2016; 7(5): 338-342 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i5/338.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i5.338>

INTRODUCTION

Gluteal compartment syndrome (GCS) is a rare condition. It may present after prolonged immobilization^[1] or after surgical procedures^[2-4]. In this report, we present a case of gluteal muscle strain with hematoma formation, secondary bacterial superinfection by methicillin-resistant *Staphylococcus aureus* (MRSA), leading to elevated compartment pressures, resulting in acute GCS. This led to rhabdomyolysis and acute kidney injury. This combination of diagnoses has not previously been reported in the literature.

CASE REPORT

A 36-year-old healthcare professional presented with increasing right buttock pain, swelling and stiffness for two days. Six days prior, he performed stiff-leg deadlifts with 295lbs, and 2 d prior, he performed seated cable rows with 240lbs. This was an increase from his normal routine. After the cable rows, he developed increasing right buttock pain and swelling and a limp. He had no fever, chills or paresthesias and denied a history of penetrating trauma, use of intramuscular anabolic agents or personal or family history of bleeding diathesis. His past medical history was significant for acute disseminated encephalomyelitis at 24-25 years of age, treated with steroids and intravenous immunoglobulins for 6 mo. Because of this, he had persistent diminished sensation from the T6 dermatome distally. There were no previous episodes of sepsis following dentistry or innocuous trauma.

At the emergency department, he had 40.4 °C fever, pulse rate was 124 bpm, respiratory rate was 22 bpm, blood pressure was 131/60 mmHg. Examination revealed warm, erythematous, tender, hard swelling of the right buttock. The left buttock was normal. Right hip motion was limited by pain, with flexion to 45°, abduction to 30°, and internal and external rotation in flexion to 30°. Lower extremity sensibility was symmetrical and unchanged from before. Ankle dorsiflexion and plantar flexion strength was 5/5 bilaterally. Distal pulses were symmetric. Of note, he demonstrated gross hematuria at the bedside.

Laboratory tests revealed white blood cell count 20300/ μ L (normal, 3.9-12.0), 88.9% neutrophils, erythrocyte sedimentation rate 31 mm/h (normal: 0-10) and C-reactive protein 17.7 mg/dL (normal: 0.0-0.8). Creatine kinase (CK) was 740/ μ L (normal: 21-232, Figure 1A), and potassium was 5.0 mmol/L (normal: 3.5-5.3), ionized calcium was 3.1 mg/dL (normal: 4.2-5.4), phosphate was 2.3 mg/dL (normal: 3.0-4.5) and blood urea nitrogen/creatinine ratio was 11.6 (normal: 12-20), suggestive of rhabdomyolysis. Lactic acid was 2.3 mEq/L (normal: 0.5-2.2), creatinine was 1.72 mg/dL (normal: 0.5-1.5, Figure 1B). Urinalysis revealed moderate blood on macroscopic exam, but only 3 red blood cells/high-power field on microscopic exam, consistent with myoglobinuria.

Radiographs were unremarkable. Magnetic resonance imaging showed gluteus maximus swelling and increased T2 signal, consistent with a high-grade muscle strain, and a central 13 cm \times 5 cm area of non-enhancement, suggestive of a hematoma (Figure 2). There was no hip joint effusion. A single dose of vancomycin and ceftriaxone was administered in the emergency room. Gluteal compartment pressures measured with the Stryker intra-compartmental pressure monitor (Stryker Surgical, Kalamazoo, MI) revealed compartment pressures of 58 mmHg and 4 mmHg for the right and left sides, respectively.

In the operating room, the gluteus maximus compartment was released using a Kocher-Langenbeck incision. Gross purulence was noted (Figure 3). Fascia over the tensor fascia lata (TFL) and gluteus medius was released and these 2 compartments were found to be uninvolved. The wound was irrigated and packed with wet-to-dry dressings. He was transferred to the intensive care unit for hydration and monitoring of renal function and serial CK (Figure 2). Intraoperative cultures revealed MRSA. Blood cultures were negative. Nasal cultures were negative for MRSA. He was started on vancomycin, cefepime and metronidazole after intraoperative cultures and adjusted to clindamycin based on final sensitivities.

He underwent repeat exploration, irrigation and debridement 2 d later. Necrotic, non-contractile gluteal muscle and cloudy interstitial fluid was noted. A necklace of antibiotic beads (Cobalt PMMA cement, Biomet, Warsaw, IN and 4 g of vancomycin powder) was placed and the wound was dressed with Ioban (3M, St Paul, MN). He underwent a third exploration 3 d later. The wound was clean and delayed primary closure was performed.

He was discharged the following day and seen in the office 10 d later. The incision had healed with no recurrence. He was discharged from further follow-up.

DISCUSSION

This patient had a unique combination of: (1) unilateral GCS; (2) MRSA infection of a hematoma; and (3) rhabdomyolysis and acute kidney injury following weightlifting.

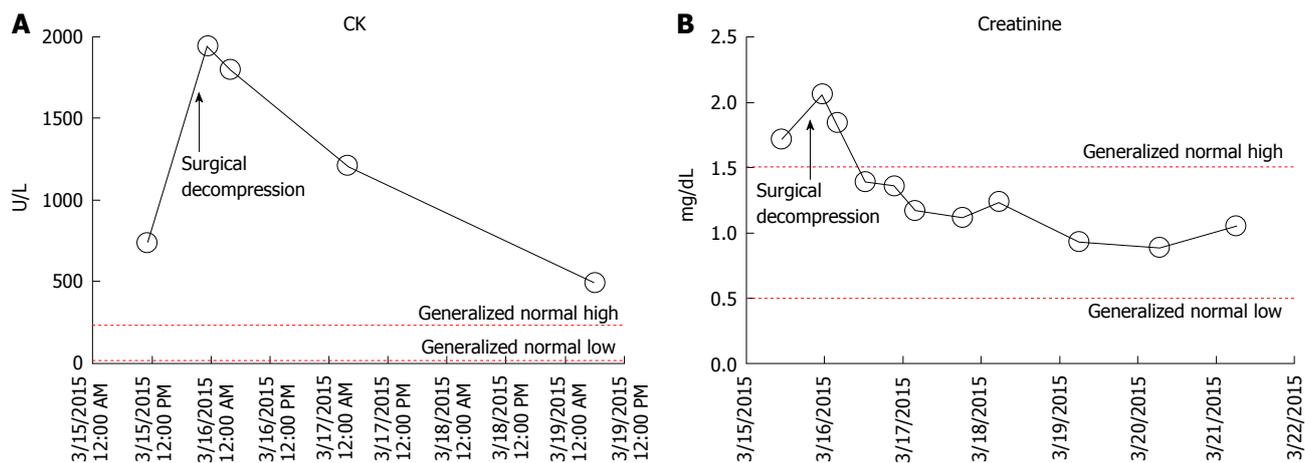


Figure 1 Graph of serum creatine kinase with time, showing (A) rapid normalization following surgical decompression, and (B) normalization following surgical decompression and aggressive hydration. CK: Creatine kinase.

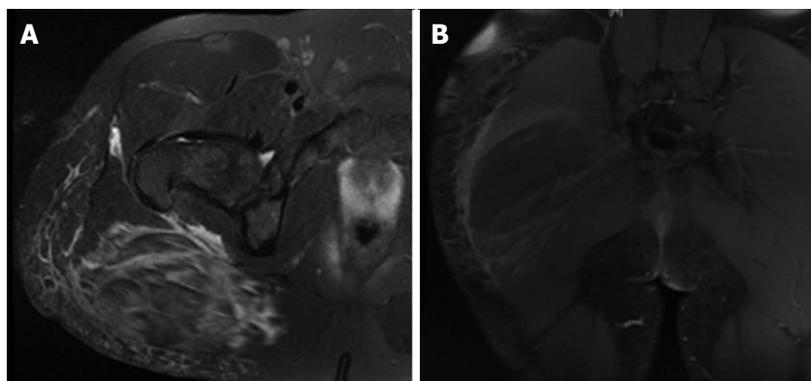


Figure 2 Magnetic resonance image. A: Axial PD FS MR image showing increased T2 signal in the gluteus maximus, with fluid extension to the trochanteric bursa and semitendinosus bursa, fluid in the deep fascia, and subcutaneous edema. There was no hip joint effusion; B: Coronal contrast-enhanced RT FS MR image showing a central 13 cm × 5 cm area of non-enhancement in the gluteus maximus, suggestive of a hematoma. MR: Magnetic resonance.

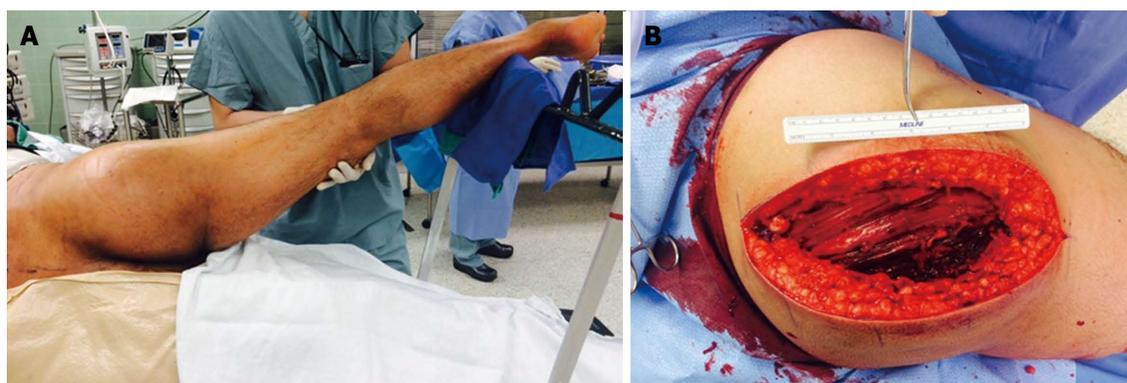


Figure 3 Intraoperative photograph (A) showing buttock swelling prior to surgical release, and (B) following surgical decompression.

Possible explanations include: (1) Acute muscle strain with expanding hematoma and bacterial superinfection, leading to elevated intracompartmental pressures; (2) Acute exertional compartment syndrome from acute muscle hypertrophy, causing GCS and late bacterial superinfection; (3) MRSA pyomyositis leading to GCS, and muscle ischemia; (4) Valsalva-related arteriole rupture, leading to an expanding hematoma, elevated

intracompartmental pressures and muscle ischemia, and subsequent bacterial superinfection; and (5) Surreptitious intramuscular injection of anabolic agents (which he vehemently denies), community-acquired MRSA superinfection, late compartment syndrome and muscle necrosis. All these hypotheses share a final common pathway of elevated compartment pressures, muscle necrosis and rhabdomyolytic kidney injury.

The temporal relationship of events leads us to believe that the first scenario is the most likely. Acute exertional compartment syndrome is unlikely as he would have presented within hours of exertion with overwhelming signs of compartment syndrome.

This combination of findings has not been reported in the literature. GCS occurs most commonly following immobilization^[1,5] because of diminished consciousness related to alcohol or illicit drugs^[6], or prolonged surgery, e.g., knee arthroplasty^[2], hip arthroplasty^[3], abdominal aortic aneurysm repair^[7], and bariatric surgery^[8]. Less common causes include falls and blunt trauma^[9], intramuscular injections^[10], and aerobic exercise^[11].

Infected GCS can occur in tropical pyomyositis^[12]. *Staphylococcus aureus* is responsible for > 75% of cases and the quadriceps, iliopsoas and gluteal muscles are most commonly affected. In these cases, it is believed that exercise elevates intracompartmental pressure with subsequent bacterial seeding^[12]. Infected GCS can also occur with Group A *Streptococcus pyogenes* (GAS) infection. This usually occurs in immunocompetent individuals and mortality is lower than expected (15%) with other GAS infections because of earlier detection and debridement^[13].

Iatrogenic bacterial seeding causing GCS can occur after intramuscular injection^[10] or acupuncture. The risk is increased in anticoagulated patients, patients with bleeding diathesis, immunocompromised patients, and those with diabetes mellitus.

Acute exertional rhabdomyolysis, acute renal failure, and myoglobinuria after GCS, usually involves multiple other limb compartments^[11]. Here, exercise-induced dehydration leads to rhabdomyolysis, while subsequent aggressive fluid resuscitation leads to limb swelling^[11].

The diagnosis of GCS was made with needle manometry. David *et al.*^[14] described the entry points for manometry in the gluteus maximus, gluteus medius-minimus, and the TFL compartments^[5]. Most authors advocate using either absolute compartment pressures > 30 mmHg or delta *P* < 30 mmHg as thresholds for surgical decompression.

The Kocher-Langenbeck incision provides excellent access to all 3 compartments and preserves femoral head vascularity^[14]. Should greater exposure be required, Henry's "question mark" incision and medial reflection of the gluteus maximus as a "gluteal lid" is a feasible alternative^[15]. Buttock soft tissue is pliable, well vascularized and mobile. Delayed primary closure is usually possible. Closure by secondary intention or skin grafting is almost never necessary. Rapid resolution of CK (Figure 1) after fasciotomy is an indicator of successful decompression^[11].

COMMENTS

Case characteristics

This patient presented with right buttock pain and swelling after working out.

Clinical diagnosis

Examination revealed tender, hard swelling of the right buttock.

Differential diagnosis

Differential diagnoses includes compartment syndrome, myositis, cellulitis, necrotizing fasciitis, abscess, septic arthritis, deep vein thrombosis.

Laboratory diagnosis

Elevated serum white blood cell count with left shift, elevated erythrocyte sedimentation rate and C-reactive protein, elevated creatine kinase, potassium, creatinine and lactic acid.

Imaging diagnosis

Magnetic resonance imaging showed gluteus maximus swelling and hematoma.

Pathological diagnosis

Compartment pressures monitoring revealed elevated gluteal compartment pressures.

Treatment

Urgent surgical debridement, fasciotomy and intravenous antibiotics.

Related reports

Gluteal compartment syndrome (GCS) is rare but presents with similar physical findings as compartment syndromes of the leg, thigh and upper extremity. If constitutional signs and signs of local sepsis are present, suspect infected compartment syndrome.

Experiences and lessons

With methicillin-resistant *Staphylococcus aureus* (MRSA) superinfection of GCS urgent debridement is necessary to prevent systemic septicemia and tissue necrosis.

Peer-review

The manuscript on the management of the gluteal compartment syndrome due to MRSA infection and abscess is interesting, well-written and does have educational value to both practicing and trainee surgeons.

REFERENCES

- 1 **Mustafa NM**, Hyun A, Kumar JS, Yekkirala L. Gluteal compartment syndrome: a case report. *Cases J* 2009; **2**: 190 [PMID: 19946500 DOI: 10.1186/1757-1626-2-190]
- 2 **Osteen KD**, Haque SH. Bilateral gluteal compartment syndrome following right total knee revision: a case report. *Ochsner J* 2012; **12**: 141-144 [PMID: 22778678]
- 3 **Kumar V**, Saeed K, Panagopoulos A, Parker PJ. Gluteal compartment syndrome following joint arthroplasty under epidural anaesthesia: a report of 4 cases. *J Orthop Surg (Hong Kong)* 2007; **15**: 113-117 [PMID: 17429132]
- 4 **Pai VS**. Compartment syndrome of the buttock following a total hip arthroplasty. *J Arthroplasty* 1996; **11**: 609-610 [PMID: 8872583 DOI: 10.1016/S0883-5403(96)80117-3]
- 5 **Taylor BC**, Dimitris C, Tancevski A, Tran JL. Gluteal compartment syndrome and superior gluteal artery injury as a result of simple hip dislocation: a case report. *Iowa Orthop J* 2011; **31**: 181-186 [PMID: 22096439]
- 6 **Liu HL**, Wong DS. Gluteal compartment syndrome after prolonged immobilisation. *Asian J Surg* 2009; **32**: 123-126 [PMID: 19423461 DOI: 10.1016/S1015-9584(09)60023-3]
- 7 **Chew MH**, Xu GG, Ho PW, Lee CW. Gluteal compartment syndrome following abdominal aortic aneurysm repair: a case report. *Ann Vasc Surg* 2009; **23**: 535.e15-535.e20 [PMID: 18834705]
- 8 **Bostanjian D**, Anthonie GJ, Hamoui N, Crookes PF. Rhabdomyolysis of gluteal muscles leading to renal failure: a potentially fatal complication of surgery in the morbidly obese. *Obes Surg* 2003; **13**: 302-305 [PMID: 12740144 DOI: 10.1381/096089203764467261]
- 9 **Brumback RJ**. Traumatic rupture of the superior gluteal artery, without fracture of the pelvis, causing compartment syndrome of

- the buttock. A case report. *J Bone Joint Surg Am* 1990; **72**: 134-137 [PMID: 2295663]
- 10 **Kühle JW**, Swoboda B. [Gluteal compartment syndrome after intramuscular gluteal injection]. *Z Orthop Ihre Grenzgeb* 1999; **137**: 366-367 [PMID: 11051025 DOI: 10.1055/s-2008-1039727]
- 11 **Kuklo TR**, Tis JE, Moores LK, Schaefer RA. Fatal rhabdomyolysis with bilateral gluteal, thigh, and leg compartment syndrome after the Army Physical Fitness Test. A case report. *Am J Sports Med* 2000; **28**: 112-116 [PMID: 10653554]
- 12 **Lamdan R**, Silverstein E, Feder HM, MacGilpin D. Tropical pyomyositis of the hip short external rotators associated with elevated intra compartmental pressure. *Orthopedics* 2008; **31**: 398 [PMID: 19292270 DOI: 10.3928/01477447-20080401-21]
- 13 **Kleshinski J**, Bittar S, Wahlquist M, Ebraheim N, Duggan JM. Review of compartment syndrome due to group A streptococcal infection. *Am J Med Sci* 2008; **336**: 265-269 [PMID: 18794622 DOI: 10.1097/MAJ.0b013e318165650a]
- 14 **David V**, Thambiah J, Kagda FH, Kumar VP. Bilateral gluteal compartment syndrome. A case report. *J Bone Joint Surg Am* 2005; **87**: 2541-2545 [PMID: 16264132 DOI: 10.2106/JBJS.D.03044]
- 15 **Henry A**. Exposures in the Lower Limb. *Extensile Exposure*. 2nd ed: Churchill Livingstone, 1973: 180-190

P- Reviewer: Friedman EA, Shrestha BM, Watanabe T
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Liu SQ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 June 18; 7(6): 343-405



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

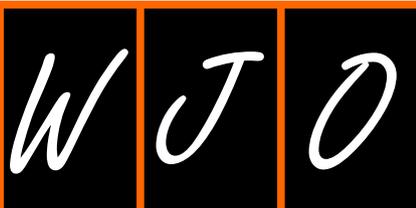
Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*



REVIEW

- 343 Current concepts in the management of recurrent anterior gleno-humeral joint instability with bone loss
Ramhamadany E, Modi CS

MINIREVIEWS

- 355 Medial ulnar collateral ligament reconstruction of the elbow in major league baseball players: Where do we stand?
Erickson BJ, Bach Jr BR, Bush-Joseph CA, Verma NN, Romeo AA
- 361 Antimicrobial technology in orthopedic and spinal implants
Eltorai AEM, Haglin J, Perera S, Brea BA, Ruttiman R, Garcia DR, Born CT, Daniels AH
- 370 Orthopedic disorders of the knee in hemophilia: A current concept review
Rodriguez-Merchan EC, Valentino LA

ORIGINAL ARTICLE

Retrospective Study

- 376 Joint arthroplasty Perioperative Surgical Home: Impact of patient characteristics on postoperative outcomes
Phan DL, Ahn K, Rinehart JB, Calderon MD, Wu WD, Schwarzkopf R

Observational Study

- 383 Quantifying prosthetic gait deviation using simple outcome measures
Kark L, Odell R, McIntosh AS, Simmons A

SYSTEMATIC REVIEWS

- 392 Allograft tissue irradiation and failure rate after anterior cruciate ligament reconstruction: A systematic review
Dashe J, Parisien RL, Cusano A, Curry EJ, Bedi A, Li X

CASE REPORT

- 401 Posterolateral dislocation of the knee: Recognizing an uncommon entity
Woon CYL, Hutchinson MR

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Antonios Angoules, MD, PhD, Assistant Lecturer, Department of Medical Laboratories, Technological Educational Institute, 11525 Athens, Greece

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Dan Li*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Xue-Mei Gong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLICATION DATE
 June 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION
<http://www.wjnet.com/esps/>

Current concepts in the management of recurrent anterior gleno-humeral joint instability with bone loss

Eamon Ramhamadany, Chetan S Modi

Eamon Ramhamadany, Chetan S Modi, Coventry and Warwickshire Shoulder and Elbow Unit, University Hospitals Coventry and Warwickshire NHS Trust, Coventry CV2 2DX, United Kingdom

Author contributions: Ramhamadany E performed the literature search, critical analysis and wrote the paper; Modi CS reviewed and edited the paper, wrote the abstract and recorded the audio core tip.

Conflict-of-interest statement: The authors declare no conflict of interest in the production of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dr. Chetan S Modi, MBChB, MSc, DipSEM, FRCS (Tr and Orth), Consultant Shoulder and Elbow Surgeon, Coventry and Warwickshire Shoulder and Elbow Unit, University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry CV2 2DX, United Kingdom. chetan.modi@uhcw.nhs.uk
Telephone: +44-2476-965094

Received: October 24, 2015
Peer-review started: October 27, 2015
First decision: February 2, 2016
Revised: February 16, 2016
Accepted: April 7, 2016
Article in press: April 11, 2016
Published online: June 18, 2016

Abstract

The management of recurrent anterior gleno-humeral joint instability is challenging in the presence of bone

loss. It is often seen in young athletic patients and dislocations related to epileptic seizures and may involve glenoid bone deficiency, humeral bone deficiency or combined bipolar lesions. It is critical to accurately identify and assess the amount and position of bone loss in order to select the most appropriate treatment and reduce the risk of recurrent instability after surgery. The current literature suggests that coracoid and iliac crest bone block transfers are reliable for treating glenoid defects. The treatment of humeral defects is more controversial, however, although good early results have been reported after arthroscopic Remplissage for small defects. Larger humeral defects may require complex reconstruction or partial resurfacing. There is currently very limited evidence to support treatment strategies when dealing with bipolar lesions. The aim of this review is to summarise the current evidence regarding the best imaging modalities and treatment strategies in managing this complex problem relating particularly to contact athletes and dislocations related to epileptic seizures.

Key words: Shoulder dislocation; Bone loss; Latarjet; Hill-Sachs lesion; Remplissage

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Managing recurrent anterior gleno-humeral instability with bone loss is challenging. Each case needs to be assessed on its own merits with consideration of both glenoid and humeral bone defects and their relative position to each other. Latarjet and iliac crest graft transfers are reliable for treating glenoid lesions. The treatment of humeral defects is controversial - the early results of Remplissage for small defects are promising; large defects may require bony reconstructions or partial resurfacing. The evidence remains limited when addressing bipolar lesions.

Ramhamadany E, Modi CS. Current concepts in the management

of recurrent anterior gleno-humeral joint instability with bone loss. *World J Orthop* 2016; 7(6): 343-354 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/343.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.343>

INTRODUCTION

Shoulder instability can be defined as a symptomatic abnormal motion of the humeral head relative to the glenoid during active shoulder motion^[1,2]. Traumatic anterior glenohumeral dislocations or subluxations can lead to recurrent instability, especially in young contact athletes and epileptic patients with humeral and/or glenoid bone loss^[3]. Failure to identify and address the bone loss when planning treatment can result in unsuccessful soft tissue stabilization procedures being performed with recurrent dislocations^[2,4]. This has been previously demonstrated by Burkhart and De Beer^[2] where 89% of contact athletes who failed soft tissue stabilization procedures were found to have significant bone loss.

Bone loss in the context of glenohumeral instability includes glenoid, humeral or combined defects. Glenoid defects are mainly located in the antero-inferior glenoid between the 2 and 6 o'clock positions^[5].

Humeral osseous defects in the context of anterior glenohumeral instability, referred to as Hill-Sachs lesions, occur where the posterolateral aspect of humeral head abuts against the anterior glenoid^[6]. Posterior dislocations are associated with reverse Hill-Sachs lesions with an impaction fracture over the anteromedial aspect of the humeral head^[3]. Co-existing osseous defects of the humerus and glenoid are termed bipolar lesions. Bipolar lesions can be defined as "on-track" or "off track", which describes the degree to which the humeral Hill-Sachs defect engages the glenoid defect in a position of 90 degrees of abduction and external rotation of the shoulder^[7].

Epidemiology

A recent population-based study by Leroux *et al*^[8] reported a 20% incidence of recurrent instability following a first time anterior shoulder dislocation in all adult patients. The highest risk group was young (< 20 years), male patients with an incidence density ratio of 98 per 100000 person-years. Other studies have also shown that young athletes and those that participate in high-energy contact sports are most likely to develop glenohumeral instability following an initial traumatic dislocation^[9,10].

Epileptic patients present as a challenging subgroup due to a tendency to develop large bipolar lesions, especially if their condition is poorly controlled^[11,12]. Bone loss in epileptic patients is also caused by underlying metabolic bone disorders with a reduced bone density seen in 20%-70% of patients taking antiepileptic medication^[13].

Several studies have analysed the incidence of bone

loss in shoulder instability. Edwards *et al*^[14] reviewed plain films of chronic anterior shoulder instability and found an osseous lesion of glenoid in 78% and humeral impaction fracture in 73%. A series of two-dimensional (2D) computed tomography (CT) scans has shown glenoid bone loss in 86% of patients with glenohumeral instability^[15]. Sugaya *et al*^[16] found a glenoid osseous defect in 50% of patients with recurrent shoulder instability. The presence of a Hill-Sachs lesion consistent with humeral bone loss in recurrent shoulder instability is estimated to be between 38% and 88%^[17,18].

There are few studies focusing on the incidence of bipolar bone loss in shoulder instability. However it should be noted that radiological studies have shown that the presence of an isolated glenoid or humeral defect increases the chances of an associated bipolar defect by a factor of 2.5 to 11^[19,20].

CLINICAL PRESENTATION AND EXAMINATION

It is important to elicit a comprehensive history when assessing patients with recurrent glenohumeral instability. One must identify the age at which the instability began and the mechanism of injury, especially of the very first dislocation. Most commonly, patients identify a traumatic injury at young age but it is important to elicit whether there has been repeated injury or trauma, particularly in athletes or epileptic patients. The direction of initial dislocation and instability must be noted as well as the position of the arm at the time of injury. In cases of recurrent instability it is the key to document the level of force required to dislocate. Indeed, patients who dislocate during low energy activity such as turning in bed, reaching out for objects, putting a coat or seatbelt on, or whilst sleeping are likely to have a greater degree of concomitant bone loss and instability. The patient may describe mechanical symptoms such as locking whilst moving their shoulder suggesting an engaging bony defect on the humeral head or glenoid. The number of instability episodes per year should be noted and whether any dislocations or subluxations needed reducing in the Emergency Department or in the operating room. It is also important to record the patient's level of function and specific tasks performed causing apprehension. Enquiring about any underlying medical conditions such as epilepsy or collagen disorders is also vital information to obtain.

Key aspects of the examination include establishing intact cuff and neurological function and any associated stiffness that may be present in chronic conditions where degenerative joint changes may already have occurred. There are a number of special tests which can be performed to assess the degree of glenohumeral instability. The load and shift helps assesses the integrity of the glenoid. The humeral head is compressed into the glenoid fossa while an anterior and posterior translation force is applied. Following bone loss the resistance to this force is lost and it is possible to dislocate or subluxate the

humeral head^[21]. The apprehension test assesses whether the patient experiences the sensation of instability when the shoulder is in the position of 90 degrees of abduction and varying degrees of external rotation. Patients with significant bone loss typically experience apprehension at lower degrees of abduction^[22]. A reducing relocation force can then be applied to see if this reduces the pain. It is also important to assess for signs of laxity: One can examine for a sulcus sign, which suggests inferior shoulder laxity. This is achieved with traction of the humerus and measuring the gap between the lateral acromion and the humeral head and comparing with the unaffected side^[23]. The Gagey hyper-abduction test looks for laxity in the inferior glenohumeral ligament and is useful to look for baseline laxity in the other/normal shoulder^[24].

INVESTIGATION AND IMAGING

Plain radiographs

Initial investigations commence with plain radiographs of the shoulder. These include a true ("turned") antero-posterior (AP), axillary and scapula Y view. Other special plain films described include the West Point View, which can demonstrate a glenoid rim fracture. The presence of a Hill-Sachs lesion can be identified with the aid of the Stryker Notch view^[22]. The Bernageau radiographic view has been described in order to calculate the degree of glenoid bone loss in glenohumeral instability^[25]. It involves taking an X-ray with the shoulder in abduction and directing the beam at 20 degrees to the horizontal, so that the antero-superior border of the glenoid is in line with the anterior line of the scapula on the image. The diameter of the glenoid is measured and compared with the healthy side to estimate bone loss. A study by Pansard *et al*^[26] however showed poor correlation with arthroscopic findings in affected individuals in a small retrospective cohort of patients with glenoid bone loss.

CT

Glenoid bone loss: Most imaging studies have focused on the evaluation of glenoid bone loss in shoulder instability. Current evidence suggests that 3D-CT is the gold standard imaging technique available to provide an accurate measure of the degree of bone loss. Chuang *et al*^[27] showed good correlation between degree of bone loss using 3D-CT with arthroscopic assessment in 188 patients.

Bishop *et al*^[28] performed a cadaveric study comparing the modalities of 2D-CT, 3D-CT and MRI to quantify bone loss and concluded that 3D-CT was the best modality to evaluate glenoid bone loss. 2D-CT relies upon orientating the beam directly perpendicular to the glenoid otherwise bone loss can be underestimated or overestimated.

There are also various different measurement techniques performed using 3D-CT to accurately quantify the glenoid defect. Several authors have concluded that

the PICO measurement technique reliably produces an accurate and reliable measure of glenoid bone loss in shoulder instability^[29-31]. The PICO method involves obtaining en-face 3D views of both the affected and normal glenoid. The healthy shoulder image is superimposed onto the affected side and the defect resembles the area of bone loss between the two. Bois concluded that 3D-CT was superior to 2D-CT and analysed three different 3D techniques to accurately quantify bone loss. The PICO method was found to be the most reliable measure of bone loss in 3D-CT^[32,33]. However, the PICO technique has a number of drawbacks including the need to scan both shoulders increasing the radiation dose. Furthermore it is unsuitable for bilateral cases as relies on the presence of a "normal" shoulder.

Sugaya *et al*^[16] reported good results in 100 patients using the "best fit circle principle". This assumes that inferior 2/3 of the glenoid resembles a "perfect circle", which has been supported by cadaveric studies^[34]. The degree of bone loss can be calculated by finding the amount of surface area missing on the affected shoulder scan^[17]. This method relies on scanning the affected shoulder alone and is currently the most widely used method.

Humeral bone loss: Studies evaluating imaging in humeral bone loss are limited. In a study of 104 patients 3D-CT was used to evaluate the parameters of the humeral Hill-Sachs defect. The use of CT with 3D reconstructions was able to accurately ascertain the size, shape and location of the defect and thereby can be predictive of humeral Hill-Sachs engagement^[35]. Chen *et al*^[36] reported that the degree of humeral bone loss can be reliably calculated by dividing the area of impaction by the total arc of the articular surface.

Ultrasonography and humeral bone loss

Ultrasound scanning has been shown to be able to detect the presence of humeral Hill-Sachs lesions^[37]. It's advantageous as it is readily available, avoids radiation, and allows one to obtain dynamic multi-planar images^[38]. Ultrasound scanning has also been shown to have a sensitivity and specificity comparable with CT arthrograms in identifying Hill-Sachs lesions^[39]. However, its limitations include operator dependence and it cannot be used to quantify the size of the humeral head defect, and thus has a limited role in pre-operative planning.

Magnetic resonance imaging

Glenoid bone loss: Magnetic resonance imaging (MRI) scanning is advantageous to CT as it allows a detailed evaluation of the soft tissues around the shoulder as well as imaging the bone. Furthermore, it avoids the risks of radiation exposure. A study of 18 cadavers revealed that the accuracy of MRI in measuring glenoid defects was comparable to CT. They used the "best circle" method previously described and applied the technique to MR^[40]. Moroder *et al*^[41] however compared

CT with MRI in 83 patients in the pre-operative planning stage to evaluate bone defects in shoulder instability and reported that CT was found to be superior in their study.

Hijusmans' cadaveric study showed good accuracy of MR arthrograms when assessing glenoid bone loss^[42]. This finding was supported in another study of 35 patients with glenoid bone loss where MR arthrograms were found to have good intra- and inter-observer reliability^[43]. Both studies showed that MR arthrograms were comparable to 3D-CT. A study by Modi *et al*^[44] with 103 patients reported that the sensitivity/specificity of MRA for glenoid bone loss was 0.58/1.00 and this increased to 0.75/1.00 when performing abduction external rotation views in addition to standard views.

Evidence to support the use of MRI is still limited and larger more significantly powered studies are required prior to it being considered equivocal to the current gold standard 3D-CT modality when trying to assess bone loss.

Humeral bone loss: Studies have reported on the ability of MRI to detect the presence of humeral Hill-Sachs lesions^[45,46]. One study considered whether MRI could accurately predict the presence of a Hill-Sachs lesion diagnosed arthroscopically: In 83 patients, 90.6% specificity and 96.3% sensitivity were reported^[46]. Evidence is limited on the ability of MRI to accurately quantify the degree of humeral bone loss. Further trials are required to evaluate this further.

MANAGEMENT

The management of bone loss in shoulder instability starts by understanding the role of patient demographics and functional demand. Failure of conservative management in glenohumeral instability has been found to be considerably higher in younger patients, especially athletes with high functional demand. A prospective study reported up to 90% recurrence rate in young athletes under 24-year-old following a first time shoulder dislocation^[47]. Specifically, participation in contact sports was a significant patient factor in developing recurrent instability^[48,49]. It is important to identify the chronicity of the shoulder problem, the functional restriction and quantification of the glenoid and humeral bone loss prior to treatment. Non-operative management in the context of bone loss in shoulder instability is reserved for high-risk surgical candidates, patients with low functional demands and those with poor compliance to rehabilitation protocols. In the specific case of patients with epilepsy, it is vital to achieve good seizure control prior to considering surgical intervention due to the high risk of surgical failure in this complex group of patients, especially as they often present with severe bipolar bone loss. We have attempted to present an algorithm, based upon the amount of glenoid and humeral bone loss, to guide management after considering the evidence currently available in the literature (Figure 1).

Glenoid bone loss

0%-25% bone loss: The literature suggests that patients with glenohumeral instability with up to 15% isolated glenoid bone loss can be treated with an arthroscopic soft tissue Bankart repair alone^[50]. Initial trials favoured open stabilization over arthroscopic Bankart repair^[51,52]. A systematic review by Brophy *et al*^[53] reported instability following arthroscopic and open Bankart repairs to be comparable. However, a study by Rhee *et al*^[54] reported a higher risk of failure with arthroscopic repair over open surgery in contact athletes although this was level 4 evidence.

In patients with 15%-25% bone loss, management is dependent on the level of functional demand of the patient. Balg *et al*^[55] devised the instability severity index score, which identified six risk factors that may predict failure of an arthroscopic soft tissue Bankart repair. These included age < 20 years, participation in contact sports, competitive level, shoulder hyperlaxity, a Hill-Sachs lesion and a loss of contour of the glenoid rim. Scoring > 6/10 on this scale predicted a 70% failure of Bankart repair in such patients.

Thus in high demand patients or those with a significantly high instability index score, effort must be made to address the bony lesion. In the acute setting, where the glenoid bony fragment can be identified, early open reduction and internal fixation of the fragment is advised. Studies have shown that open reduction and fixation of a glenoid rim fracture with screws shows good outcomes at 1 year and a high rate of union^[56,57]. Comminution and the inability to fix the fragment, necessitates a bony reconstruction procedure such as a Latarjet procedure^[21]. In contrast, lower demand patients may be successfully managed with a soft tissue Bankart procedure alone.

> 25% bone loss: Significant bone loss has been described where the glenoid takes the appearance of an "inverted pear" shape. This corresponds to at least 25% bone loss. Burkhart *et al*^[2] identified a 67% recurrent instability rate in such patients undergoing a soft tissue Bankart repair in contrast to 4% in those without bony deficiency.

In an acute setting, anatomical reduction may be achieved using open or arthroscopic reduction and internal fixation of the rim fragment. In cases where this is not possible reconstruction of the osseous defect is required. There are several ways this can be achieved including coracoid transfer procedures and the use of autografts or allografts to restore the bony anatomy of the glenoid.

Coracoid transfer procedures include the Bristow and Latarjet techniques. The Bristow procedure transfers the tip of the coracoid with its attached conjoint tendon to the anterior glenoid^[58]. The Latarjet procedure involves transfer of approximately 3 cm of the coracoid in addition to the conjoint tendon hence provides a greater bony augment and allows fixation with two screws rather than one, as with the Bristow, increasing the stability and chance of successful union^[59]. It also extends the

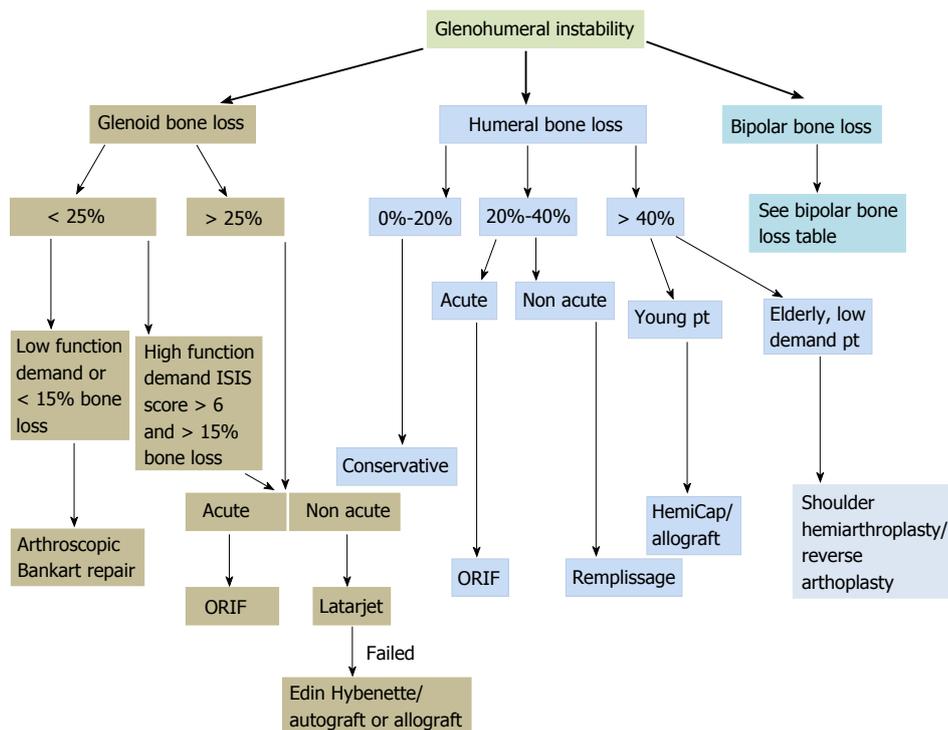


Figure 1 Management of glenoid and humeral bone loss in shoulder instability. ISIS: Instability severity index score; ORIF: Open reduction and internal fixation; pt: Patient.

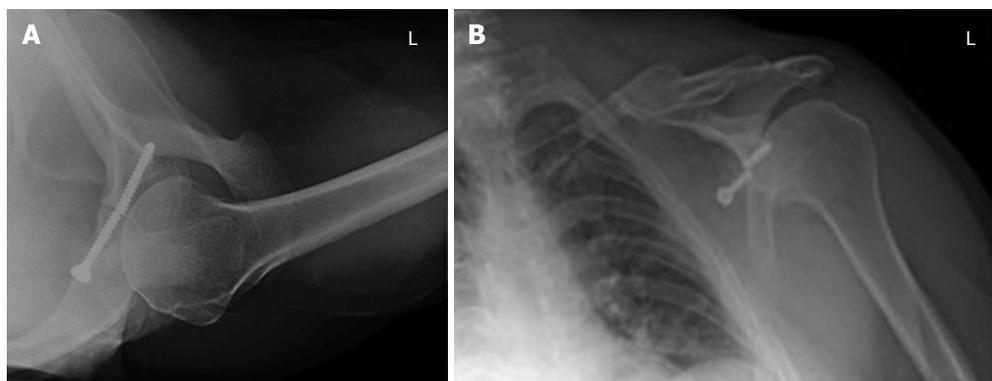


Figure 2 45-year-old gentleman with previous open Latarjet procedure for left shoulder instability. Subsequent non-union of graft and failure of metalwork is seen on the axillary (A) and antero-posterior (B) radiographs.

concavity of the glenoid articular arc increasing the ability to resist off axis loads that allow the shoulder to subluxate or dislocate^[60]. The transfer of the conjoint tendon with the graft also contributes to increased stability as it acts as a sling across the antero-inferior capsule when the shoulder is in abduction and external rotation. The original Latarjet procedure has been modified to preserve the inferior subscapularis muscle contributing to soft tissue stability. Furthermore the graft may be kept extra-articular by repair of the capsule to the native glenoid, which helps to stop the graft abrading the humeral surface^[61].

Several studies have reported good outcomes with the Latarjet procedure, with low rates of recurrent instability, high patient satisfaction and return to sports^[60,62]. Critics of the open Latarjet have focused on the loss of

external rotation post procedure, which could have an adverse impact on overhead throwing athletes, and the development of osteoarthritis^[63]. Other complications include infection, neurological injuries, non-union of the Latarjet graft and failure of metalwork (Figure 2).

A developing concept is an arthroscopic Latarjet procedure, which is a technically demanding procedure and should only be undertaken by the expert arthroscopist. Lafosse *et al*^[64] reported no recurrence in 96 patients treated with an arthroscopic Latarjet with 91% of patients reporting an excellent subjective outcome on Disabilities of Arm, Shoulder and Hand score. Boileau *et al*^[65] have advanced the technique by combining arthroscopic Latarjet with a Bankart repair (2B3 procedure). It is thought that repairing the residual capsular labrum contributes to shoulder stability and helps maintain proprioceptive fibres



Figure 3 Failed Latarjet procedure in Figure 1 treated with an Eden Hybinette procedure using an autologous iliac crest bone graft. The graft position and fixation with 2 screws is shown on the antero-posterior radiograph.

needed in athletes. Ninety-one percent of patients had no evidence of osteoarthritis with this technique, with all throwing athletes returning to sports, and only a mean 9 degree loss of external rotation on the operated side.

Glenoid reconstruction with autograft or allograft is another technique aimed at anatomically reconstructing the osseous defect. It addresses the bone defect but does not address the loss of stability caused by the laxity of the inferior glenohumeral ligament^[66]. Griffin *et al*^[3] has suggested that an autograft or allograft may be a used in cases of a failed Latarjet or in cases of concurrent coracoid fracture. It may also be of use in massive glenoid bone loss where the coracoid transfer is not enough bone stock to augment the defect.

The most commonly described autograft has been the Eden-Hybinette procedure. This involves using the inner table of the iliac crest as an autologous graft to augment the glenoid defect (Figure 3). Both intra and extra-articular grafts have been described. Studies have reported good outcomes in the use of iliac crest bone autograft in patients. However these studies are limited by small population groups and limited follow-up period^[67-69]. The use of a distal clavicle arthroscopic autograft has also been reported^[70].

Several studies have commented on the use of allografts for glenoid reconstructions. These include distal tibia^[71] and femoral head allografts^[72]. It has been proposed that the use of allografts may have several advantages over autografts including a more accurate restoration of the anatomical contour of the glenoid as well as the addition of a cartilaginous interface for articulation with the humeral head. Sayegh *et al*^[73] conducted a systematic review into the use of allografts in addressing glenoid bone loss. This study concluded a recurrence rate of instability of 7.1% following allograft procedure with excellent subjective clinical outcome. The review included a collection of small population studies hence the effectiveness and limitations of this treatment are yet to be fully understood.

It has been proposed that low demand patients may still be managed successfully with arthroscopic Bankart stabilization. Kim *et al*^[74] showed that in a study of 36

non-athletic individuals with low functional demand, arthroscopic stabilization produced a satisfactory outcome in patients with glenoid bone loss of 20%-30%. However in patients with excessive joint laxity, arthroscopic stabilization is unreliable with a recurrent instability rate of 23%. These findings are also supported by a study of 21 patients with 20%-30% bone loss by Mologne *et al*^[75]. One must be cautious with these findings, however, as both studies are poorly powered statistically with limited follow-up duration.

Humeral bone loss

0%-20% bone loss: Current concepts suggest that a humeral bone defect of 0%-20% can be managed conservatively. A trial of immobilization followed by physiotherapy focusing on dynamic shoulder stabilizers is warranted. In most individuals this will be a suitable management strategy, especially in the elderly and low demand patients^[76] (Figure 1).

It is important to understand however high demand athletes, such as baseball players, who require stability throughout extremes of motion may require surgery at a lower threshold of bone loss.

20%-40% bone loss: Various different surgical strategies have been described for managing humeral bone loss > 20%. In cases where a humeral defect has been detected within 3-4 wk of injury, anatomical fixation of the defect has been described. This involves disimpaction of the humeral defect by elevating it with a bone tap until anatomy of the head is restored. The defect can then be held with cortical screws and defect be filled with cancellous bone graft. Unfortunately there is noticeable lack of evidence in the literature focusing on this technique's outcome and indication^[77,78].

The Remplissage technique has recently become more popular for the treatment of engaging Hill-Sachs lesions. This involves a tenodesis of the infraspinatus tendon and posterior capsule into the humeral head defect rendering the defect extra-articular and thus preventing engagement with the glenoid rim^[79]. It is now usually performed arthroscopically and can be combined with a Bankart repair to address combined humeral and glenoid defects where glenoid bone loss is < 25%. Open techniques involve mobilizing the tendon free from its attachment on the greater tuberosity and suturing it into the defect over the lateral humeral cortex. In larger defects up to 40% it is advisable to osteotomise the greater tuberosity with the infraspinatus tendon and to fix the bone and tendon transfer into the defect with fully threaded cancellous screws^[80].

The reported outcomes of arthroscopic remplissage are promising. Purchase, Sahajpal *et al*^[80] reported a recurrent instability rate of 7% at 2 years post surgery with no significant loss in range of motion. Other studies report a loss of external rotation between 1.9 to 8 degrees^[81,82]. A 90% return to sport has been reported following the procedure. A systematic review comparing remplissage, weber osteotomy and allograft procedures

Table 1 Management of bipolar bone loss in shoulder instability

	Bipolar bone loss			
	Non engaging humeral Hill-Sachs "on-track"	Engaging humeral Hill-Sachs "off-track" < 40% loss	Engaging humeral Hill-Sachs "off track" large defect > 40% loss. Young pt	Engaging humeral Hill-Sachs "off track" large defect > 40% Elderly pt
Glenoid bone loss < 25%	Arthroscopic Bankart repair	Remplissage ± Bankart	HemiCap ± Bankart	Shoulder hemiarthroplasty
Glenoid bone loss > 25%	Latarjet procedure	Latarjet + remplissage	Latarjet + HemiCap	Reverse shoulder replacement

pt: Patient.

for humeral bone loss found that remplissage had the better outcome scores and fewer complications^[83].

Historically proximal rotational humeral osteotomy, described by Weber *et al*^[84] in 1969, was used to treat young adults with moderate to severe Hill-Sachs lesions with aim of restoring stability. This involved a subcapital humeral osteotomy with medial rotation of humeral head by 25 degrees and imbrication of subscapularis tendon and anterior capsule. As a result the humeral defect could not engage the glenoid through the arc of motion. However the procedure is associated with high complication rates and has fallen out of favour^[85,86].

> 40% bone loss: In young patients with large humeral defects (> 40% bone loss), osseous allograft reconstruction has been described as a useful strategy to avoid the need for prosthetic replacement. The data in the literature on this technique is very limited and further work is needed to evaluate the efficacy and limitations of technique. Miniaci *et al*^[85,86] used fresh frozen cryopreserved humeral head allografts in 18 patients. The graft is size and side matched to reconstruct the humeral head following chevron osteotomy of the Hill-Sachs defect. At 50 mo there were no episodes of instability and an 89% return to work. Two patients had partial graft failure and three showed early evidence of osteoarthritis. Another strategy has been the use of femoral head allografts. In a study of 13 patients there was a high Constant score 86.8 at 54 mo with one case of osteonecrosis noted^[87].

An emerging technique in the treatment of young patients with bone loss > 40% has been the use of a partial resurfacing prosthesis such as the HemiCAP® (Arthrosurface, Franklin, MA, United States). This uses a spherical cobalt chrome component to fill the Hill-Sachs defect and restore joint congruity. The technique requires patients to have at least 60% normal bone stock, hence is contraindicated in those with osteoporotic bone^[88]. The largest case series performed by Raiss *et al*^[89] only involved 10 patients. They performed uncemented partial resurfacing in locked anterior dislocation patients with significant humeral bone loss and found an increase Constant score of 41 points post operatively with two re-operations for dislocation and glenoid erosion. Other case reports have been discussed in the context of bipolar bone loss where the engaging humeral defect was treated with this technique^[90,91].

The lack of significant evidence in the literature sug-

gests that there is no consensus strategy as to how to treat young patients with large degrees of humeral bone loss. Shoulder hemiarthroplasty is advocated in low demand or elderly patients with osteopenic bone and young adults in whom the strategies discussed above are not appropriate. Indeed in those patients with concomitant glenoid wear it may be sensible to consider a total shoulder replacement^[92].

Bipolar humeral and glenoid bone loss

The management of bipolar or combined humeral and glenoid bone loss in the context of shoulder instability is an evolving concept. This degree of bone loss is usually seen after multiple traumatic dislocations and epileptic seizures. The key factors are the degree of bone loss involved but also whether the humeral Hill-Sachs lesion engages or not. The significance of the interaction between the humeral and glenoid defect can best be understood using the glenoid track principle. Yamamoto *et al*^[93] described the glenoid track as the zone of contact between the humeral head and the glenoid at 90 degrees of shoulder abduction relative to the trunk. The region corresponds to 83% of diameter of the glenoid and represents a distance from the medial point of the contact area to the medial margin of the rotator cuff insertion on the humerus^[94]. Thus glenoid bone loss decreases the size of the glenoid track (Table 1).

If the humeral Hill-Sachs bone lesion lies within the diameter of the glenoid track, there is bone support adjacent to this and the lesion is described as being "on-track". If the defect lies outside this region, there is no adjacent bone support and the lesion is "off track". If the Hill-Sachs lesion is "off-track" it gives rise to a more unstable shoulder in the context of bipolar bone loss. An updated definition of an engaging humeral bone lesion can be defined as one that lies outside of the glenoid track^[50].

The concepts described can help determine the management of bipolar bone loss in shoulder instability. We have previously discussed the treatment of both glenoid and humeral bone loss individually. Di Giacomo *et al*^[7] has proposed an algorithm for combined bone loss. Fundamental to this is whether the humeral bone lesion is "on track" or not. Bipolar defects with an "on-track" humeral defect may be treated by addressing the glenoid defect alone. Hence < 25% glenoid bone loss can be managed with arthroscopic Bankart repair and > 25% bone loss with a Latarjet procedure.

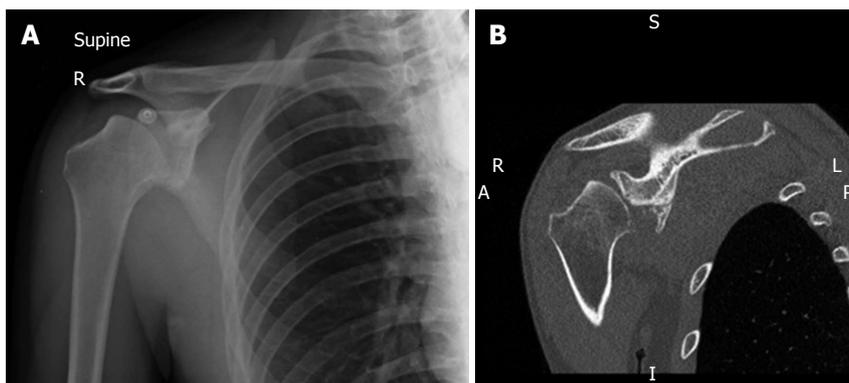


Figure 4 Antero-posterior radiograph (A) and computed tomography scan (B) of a 25-year-old epileptic with massive bipolar bone loss. He was found to have > 25% glenoid bone loss and > 40% humeral bone loss pre-operatively.

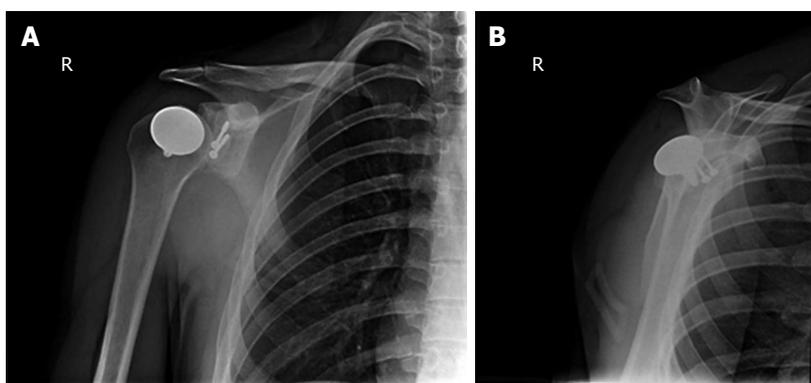


Figure 5 Antero-posterior (A) and scapular Y (B) views of an epileptic patient with massive bipolar bone loss treated with a humeral HemiCap and Latarjet procedure.

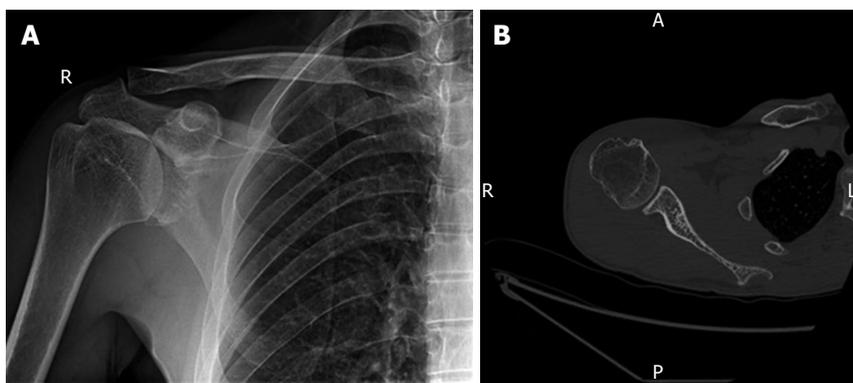


Figure 6 42-year-old manual worker with anterior shoulder instability with < 25% glenoid bone loss and an engaging Hill-Sachs lesion. He was managed successfully with an arthroscopic Remplissage and Bankart repair. Pre-operative antero-posterior radiographs (A) and computed tomography (B) images are demonstrated.

Patients with an “off-track” humeral bone defect require both the glenoid and the humeral defect to be addressed. Ranne *et al*^[25] described successfully combining an open Latarjet and Remplissage in a patient with severe bipolar bone loss. This may be a reasonable option in those with > 25% glenoid bone loss with engaging humeral defects. In cases with significant > 40% humeral bone loss and > 25% glenoid loss, treatment with a combination of an open Latarjet with a partial resurfacing/replacement or allograft reconstruction

procedure would address both the glenoid and humeral bone loss respectively (Figures 4 and 5). Those, however, with a lesser degree of glenoid bone loss < 25% with an “off-track” humeral Hill-Sachs may be successfully treated with a combined arthroscopic Bankart and Remplissage procedure (Figure 6).

In the case of failure of such procedures, the only available options for salvage surgery may be to consider shoulder fusion in younger patients (Figure 7), and reverse shoulder arthroplasty is older, lower demand

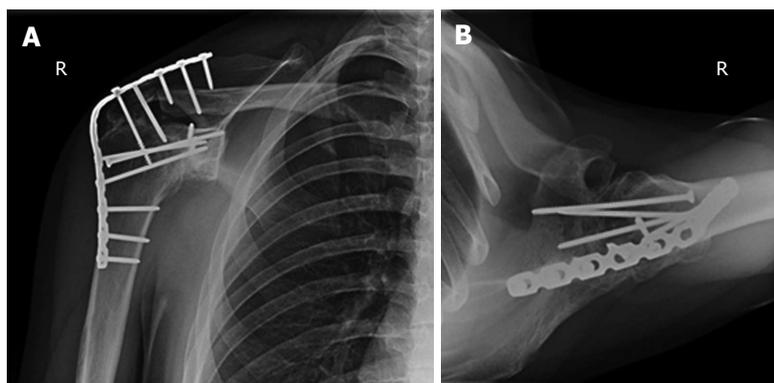


Figure 7 Antero-posterior (A) and axillary view (B) radiographs six months following shoulder fusion after failure of a combined HemiCap and Latarjet procedure in an epileptic patient with massive bipolar bone loss.

patients to restore stability and maintain some function.

CONCLUSION

Bone loss in shoulder instability is a challenging problem to orthopaedic clinicians. In this review we have addressed the current concepts in identifying and treating such patients using best current evidence available. Currently the literature is limited and further high level evidence studies are needed to further investigate the benefit of different surgical strategies, particularly in the area of combined humeral and glenoid bone loss.

REFERENCES

- 1 **Kreitner KF**, Mähringer-Kunz A. [Systematics of shoulder instability]. *Radiologe* 2015; **55**: 195-202 [PMID: 25672912 DOI: 10.1007/s00117-014-2784-6]
- 2 **Burkhart SS**, De Beer JF. Traumatic glenohumeral bone defects and their relationship to failure of arthroscopic Bankart repairs: significance of the inverted-pear glenoid and the humeral engaging Hill-Sachs lesion. *Arthroscopy* 2000; **16**: 677-694 [PMID: 11027751 DOI: 10.1053/jars.2000.17715]
- 3 **Griffin JW**, Brockmeier SF. Shoulder instability with concomitant bone loss in the athlete. *Orthop Clin North Am* 2015; **46**: 89-103 [PMID: 25435038 DOI: 10.1016/j.ocl.2014.09.006]
- 4 **Bigliani LU**, Newton PM, Steinmann SP, Connor PM, McIlveen SJ. Glenoid rim lesions associated with recurrent anterior dislocation of the shoulder. *Am J Sports Med* 1998; **26**: 41-45 [PMID: 9474399]
- 5 **Piasecki DP**, Verma NN, Romeo AA, Levine WN, Bach BR, Provencher MT. Glenoid bone deficiency in recurrent anterior shoulder instability: diagnosis and management. *J Am Acad Orthop Surg* 2009; **17**: 482-493 [PMID: 19652030]
- 6 **Provencher MT**, Frank RM, Leclere LE, Metzger PD, Ryu JJ, Bernhardson A, Romeo AA. The Hill-Sachs lesion: diagnosis, classification, and management. *J Am Acad Orthop Surg* 2012; **20**: 242-252 [PMID: 22474094 DOI: 10.5435/JAAOS-20-04-242]
- 7 **Di Giacomo G**, Itoi E, Burkhart SS. Evolving concept of bipolar bone loss and the Hill-Sachs lesion: from “engaging/non-engaging” lesion to “on-track/off-track” lesion. *Arthroscopy* 2014; **30**: 90-98 [PMID: 24384275 DOI: 10.1016/j.arthro.2013.10.004]
- 8 **Leroux T**, Wasserstein D, Veillette C, Khoshbin A, Henry P, Chahal J, Austin P, Mahomed N, Ogilvie-Harris D. Epidemiology of primary anterior shoulder dislocation requiring closed reduction in Ontario, Canada. *Am J Sports Med* 2014; **42**: 442-450 [PMID: 24275862 DOI: 10.1177/0363546513510391]
- 9 **Owens BD**, Agel J, Mountcastle SB, Cameron KL, Nelson BJ. Incidence of glenohumeral instability in collegiate athletics. *Am J*

- Sports Med* 2009; **37**: 1750-1754 [PMID: 19556471 DOI: 10.1177/0363546509334591]
- 10 **Hovelius L**, Augustini BG, Fredin H, Johansson O, Norlin R, Thorling J. Primary anterior dislocation of the shoulder in young patients. A ten-year prospective study. *J Bone Joint Surg Am* 1996; **78**: 1677-1684 [PMID: 8934481]
- 11 **Goudie EB**, Murray IR, Robinson CM. Instability of the shoulder following seizures. *J Bone Joint Surg Br* 2012; **94**: 721-728 [PMID: 22628584 DOI: 10.1302/0301-620X.94B6.28259]
- 12 **Bühler M**, Gerber C. Shoulder instability related to epileptic seizures. *J Shoulder Elbow Surg* 2002; **11**: 339-344 [PMID: 12195251 DOI: 10.1067/mse.2002.124524]
- 13 **Petty SJ**, O'Brien TJ, Wark JD. Anti-epileptic medication and bone health. *Osteoporos Int* 2007; **18**: 129-142 [PMID: 17091219 DOI: 10.1007/s00198-006-0185-z]
- 14 **Edwards TB**, Boulahia A, Walch G. Radiographic analysis of bone defects in chronic anterior shoulder instability. *Arthroscopy* 2003; **19**: 732-739 [PMID: 12966381 DOI: 10.1016/S0749-8063(03)00684-4]
- 15 **Griffith JF**, Antonio GE, Yung PS, Wong EM, Yu AB, Ahuja AT, Chan KM. Prevalence, pattern, and spectrum of glenoid bone loss in anterior shoulder dislocation: CT analysis of 218 patients. *AJR Am J Roentgenol* 2008; **190**: 1247-1254 [PMID: 18430839 DOI: 10.2214/AJR.07.3009]
- 16 **Sugaya H**, Moriishi J, Dohi M, Kon Y, Tsuchiya A. Glenoid rim morphology in recurrent anterior glenohumeral instability. *J Bone Joint Surg Am* 2003; **85-A**: 878-884 [PMID: 12728039]
- 17 **Itoi E**, Yamamoto N, Omori Y. Glenoid track. In: Di Giacomo G, Costantini A, De Vita A, de Gasperis N, editors. *Shoulder Instability: Alternative Surgical Techniques*. New York, NY, USA: Springer, 2011
- 18 **Rowe CR**. Acute and recurrent anterior dislocations of the shoulder. *Orthop Clin North Am* 1980; **11**: 253-270 [PMID: 7001307]
- 19 **Horst K**, Von Harten R, Weber C, Andruszkow H, Pfeifer R, Dienstknecht T, Pape HC. Assessment of coincidence and defect sizes in Bankart and Hill-Sachs lesions after anterior shoulder dislocation: a radiological study. *Br J Radiol* 2014; **87**: 20130673 [PMID: 24452107 DOI: 10.1259/bjr.20130673]
- 20 **Widjaja AB**, Tran A, Bailey M, Proper S. Correlation between Bankart and Hill-Sachs lesions in anterior shoulder dislocation. *ANZ J Surg* 2006; **76**: 436-438 [PMID: 16768763 DOI: 10.1111/j.1445-2197.2006.03760.x]
- 21 **Schrumpf MA**, Maak TG, Delos D, Jones KJ, Dines DM, Walch G, Dines JS. The management of anterior glenohumeral instability with and without bone loss: AAOS exhibit selection. *J Bone Joint Surg Am* 2014; **96**: e12 [PMID: 24430421 DOI: 10.2106/JBJS.L.01377]
- 22 **Bushnell BD**, Creighton RA, Herring MM. The bony apprehension test for instability of the shoulder: a prospective pilot analysis. *Arthroscopy* 2008; **24**: 974-982 [PMID: 18760203 DOI: 10.1016/j.arthro.2008.07.019]
- 23 **Neer CS**, Foster CR. Inferior capsular shift for involuntary inferior

- and multidirectional instability of the shoulder. A preliminary report. *J Bone Joint Surg Am* 1980; **62**: 897-908 [PMID: 7430177]
- 24 **Gagey OJ**, Gagey N. The hyperabduction test. *J Bone Joint Surg Br* 2001; **83**: 69-74 [PMID: 11245541 DOI: 10.1302/0301-620X.83B1.10628]
- 25 **Ranne JO**, Sarimo JJ, Heinonen OJ, Orava SY. A combination of Latarjet and Remplissage for treatment of severe glenohumeral instability and bone loss. A case report. *J Orthop* 2013; **10**: 46-48 [PMID: 24403748 DOI: 10.1016/j.jor.2013.01.007]
- 26 **Pansard E**, Klouche S, Billot N, Rousselin B, Kraus TM, Bauer T, Hardy P. Reliability and validity assessment of a glenoid bone loss measurement using the Bernageau profile view in chronic anterior shoulder instability. *J Shoulder Elbow Surg* 2013; **22**: 1193-1198 [PMID: 23473607 DOI: 10.1016/j.jse.2012.12.032]
- 27 **Chuang TY**, Adams CR, Burkhart SS. Use of preoperative three-dimensional computed tomography to quantify glenoid bone loss in shoulder instability. *Arthroscopy* 2008; **24**: 376-382 [PMID: 18375267 DOI: 10.1016/j.arthro.2007.10.008]
- 28 **Bishop JY**, Jones GL, Rerko MA, Donaldson C. 3-D CT is the most reliable imaging modality when quantifying glenoid bone loss. *Clin Orthop Relat Res* 2013; **471**: 1251-1256 [PMID: 22996361 DOI: 10.1007/s11999-012-2607-x]
- 29 **Magarelli N**, Milano G, Sergio P, Santagada DA, Fabbriani C, Bonomo L. Intra-observer and interobserver reliability of the 'Pico' computed tomography method for quantification of glenoid bone defect in anterior shoulder instability. *Skeletal Radiol* 2009; **38**: 1071-1075 [PMID: 19466406 DOI: 10.1007/s00256-009-0719-5]
- 30 **Magarelli N**, Milano G, Baudi P, Santagada DA, Righi P, Spina V, Leone A, Amelia R, Fabbriani C, Bonomo L. Comparison between 2D and 3D computed tomography evaluation of glenoid bone defect in unilateral anterior gleno-humeral instability. *Radiol Med* 2012; **117**: 102-111 [PMID: 21744248 DOI: 10.1007/s11547-011-0712-7]
- 31 **d'Elia G**, Di Giacomo A, D'Alessandro P, Cirillo LC. Traumatic anterior glenohumeral instability: quantification of glenoid bone loss by spiral CT. *Radiol Med* 2008; **113**: 496-503 [PMID: 18493827 DOI: 10.1007/s11547-008-0274-5]
- 32 **Bois AJ**, Fening SD, Polster J, Jones MH, Miniaci A. Quantifying glenoid bone loss in anterior shoulder instability: reliability and accuracy of 2-dimensional and 3-dimensional computed tomography measurement techniques. *Am J Sports Med* 2012; **40**: 2569-2577 [PMID: 23019250 DOI: 10.1177/0363546512458247]
- 33 **Baudi P**, Campochiaro G, Rebuzzi M, Matino G, Catani F. Assessment of bone defects in anterior shoulder instability. *Joints* 2013; **1**: 40-48 [PMID: 25785257]
- 34 **De Wilde LF**, Berghs BM, Audenaert E, Sys G, Van Maele GO, Barbaix E. About the variability of the shape of the glenoid cavity. *Surg Radiol Anat* 2004; **26**: 54-59 [PMID: 14504818 DOI: 10.1007/s00276-003-0167-1]
- 35 **Cho SH**, Cho NS, Rhee YG. Preoperative analysis of the Hill-Sachs lesion in anterior shoulder instability: how to predict engagement of the lesion. *Am J Sports Med* 2011; **39**: 2389-2395 [PMID: 21398576 DOI: 10.1177/0363546511398644]
- 36 **Chen AL**, Hunt SA, Zuckerman JD. "Humeral head impression fractures and head-splitting fractures." In: *Shoulder Fractures: The Practical Guide to Management*. Zuckerman JD, Koval KJ, editors. New York, 2005: 120-143
- 37 **Hammar MV**, Wintzell GB, Aström KG, Larsson S, Elvin A. Role of us in the preoperative evaluation of patients with anterior shoulder instability. *Radiology* 2001; **219**: 29-34 [PMID: 11274531 DOI: 10.1148/radiology.219.1.r01mr1329]
- 38 **Cicak N**, Bilić R, Delimar D. Hill-Sachs lesion in recurrent shoulder dislocation: sonographic detection. *J Ultrasound Med* 1998; **17**: 557-560 [PMID: 9733173]
- 39 **Farin PU**, Kaukanen E, Jaroma H, Harju A, Väättäin U. Hill-Sachs lesion: sonographic detection. *Skeletal Radiol* 1996; **25**: 559-562 [PMID: 8865491 DOI: 10.1007/s002560050135]
- 40 **Gyftopoulos S**, Hasan S, Bencardino J, Mayo J, Nayyar S, Babb J, Jazrawi L. Diagnostic accuracy of MRI in the measurement of glenoid bone loss. *AJR Am J Roentgenol* 2012; **199**: 873-878 [PMID: 22997381 DOI: 10.2214/AJR.11.7639]
- 41 **Moroder P**, Resch H, Schnaitmann S, Hoffelner T, Tauber M. The importance of CT for the pre-operative surgical planning in recurrent anterior shoulder instability. *Arch Orthop Trauma Surg* 2013; **133**: 219-226 [PMID: 23179478 DOI: 10.1007/s00402-012-1656-7]
- 42 **Huysmans PE**, Haen PS, Kidd M, Dhert WJ, Willems JW. The shape of the inferior part of the glenoid: a cadaveric study. *J Shoulder Elbow Surg* 2006; **15**: 759-763 [PMID: 16990019 DOI: 10.1016/j.jse.2005.09.001]
- 43 **Markenstein JE**, Jaspars KC, van der Hulst VP, Willems WJ. The quantification of glenoid bone loss in anterior shoulder instability; MR-arthro compared to 3D-CT. *Skeletal Radiol* 2014; **43**: 475-483 [PMID: 24442561 DOI: 10.1007/s00256-013-1780-7]
- 44 **Modi CS**, Karthikeyan S, Marks A, Saithna A, Smith CD, Rai SB, Drew SJ. Accuracy of abduction-external rotation MRA versus standard MRA in the diagnosis of intra-articular shoulder pathology. *Orthopedics* 2013; **36**: e337-e342 [PMID: 23464954 DOI: 10.3928/01477447-20130222-23]
- 45 **Probyn LJ**, White LM, Salonen DC, Tomlinson G, Boynton EL. Recurrent symptoms after shoulder instability repair: direct MR arthrographic assessment--correlation with second-look surgical evaluation. *Radiology* 2007; **245**: 814-823 [PMID: 17951350 DOI: 10.1148/radiol.2453061329]
- 46 **Hayes ML**, Collins MS, Morgan JA, Wenger DE, Dahm DL. Efficacy of diagnostic magnetic resonance imaging for articular cartilage lesions of the glenohumeral joint in patients with instability. *Skeletal Radiol* 2010; **39**: 1199-1204 [PMID: 20411385 DOI: 10.1007/s00256-010-0922-4]
- 47 **Taylor DC**, Arciero RA. Pathologic changes associated with shoulder dislocations. Arthroscopic and physical examination findings in first-time, traumatic anterior dislocations. *Am J Sports Med* 1997; **25**: 306-311 [PMID: 9167808 DOI: 10.1177/036354659702500306]
- 48 **Pagnani MJ**, Dome DC. Surgical treatment of traumatic anterior shoulder instability in american football players. *J Bone Joint Surg Am* 2002; **84-A**: 711-715 [PMID: 12004010]
- 49 **Zaffagnini S**, Marcheggiani Muccioli GM, Giordano G, Bonanzinga T, Grassi A, Nitri M, Bruni D, Ravazzolo G, Marcacci M. Long-term outcomes after repair of recurrent post-traumatic anterior shoulder instability: comparison of arthroscopic transglenoid suture and open Bankart reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 816-821 [PMID: 21932077 DOI: 10.1007/s00167-011-1674-y]
- 50 **Kurokawa D**, Yamamoto N, Nagamoto H, Omori Y, Tanaka M, Sano H, Itoi E. The prevalence of a large Hill-Sachs lesion that needs to be treated. *J Shoulder Elbow Surg* 2013; **22**: 1285-1289 [PMID: 23466174 DOI: 10.1016/j.jse.2012.12.033]
- 51 **Guanche CA**, Quick DC, Sodergren KM, Buss DD. Arthroscopic versus open reconstruction of the shoulder in patients with isolated Bankart lesions. *Am J Sports Med* 1996; **24**: 144-148 [PMID: 8775110]
- 52 **Geiger DF**, Hurley JA, Tovey JA, Rao JP. Results of arthroscopic versus open Bankart suture repair. *Clin Orthop Relat Res* 1997; **337**: 111-117 [PMID: 9137182 DOI: 10.1097/00003086-199704000-00013]
- 53 **Prophy RH**, Marx RG. The treatment of traumatic anterior instability of the shoulder: nonoperative and surgical treatment. *Arthroscopy* 2009; **25**: 298-304 [PMID: 19245994 DOI: 10.1016/j.arthro.2008.12.007]
- 54 **Rhee YG**, Ha JH, Cho NS. Anterior shoulder stabilization in collision athletes: arthroscopic versus open Bankart repair. *Am J Sports Med* 2006; **34**: 979-985 [PMID: 16436537 DOI: 10.1177/0363546505283267]
- 55 **Balg F**, Boileau P. The instability severity index score. A simple pre-operative score to select patients for arthroscopic or open shoulder stabilisation. *J Bone Joint Surg Br* 2007; **89**: 1470-1477 [PMID: 17998184 DOI: 10.1302/0301-620X.89B11.18962]
- 56 **Frush TJ**, Hasan SS. Arthroscopic reduction and cannulated screw fixation of a large anterior glenoid rim fracture. *J Shoulder Elbow Surg* 2010; **19**: e16-e19 [PMID: 20189417 DOI: 10.1016/j.jse.2009.11.001]

- 57 **Park JY**, Lee SJ, Lhee SH, Lee SH. Follow-up computed tomography arthrographic evaluation of bony Bankart lesions after arthroscopic repair. *Arthroscopy* 2012; **28**: 465-473 [PMID: 22265046 DOI: 10.1016/j.arthro.2011.09.008]
- 58 **May VR**. A modified Bristow operation for anterior recurrent dislocation of the shoulder. *J Bone Joint Surg Am* 1970; **52**: 1010-1016 [PMID: 5479471]
- 59 **Allain J**, Goutallier D, Glorion C. Long-term results of the Latarjet procedure for the treatment of anterior instability of the shoulder. *J Bone Joint Surg Am* 1998; **80**: 841-852 [PMID: 9655102]
- 60 **Patte D**, Bernageau J, Bancel P. The anteroinferior vulnerable point of the glenoid rim. In: Bateman JE, Welch RP, editors. Surgery of the shoulder. New York: Marcel Dekker, 1985: 94-99
- 61 **Burkhart SS**, De Beer JF, Barth JR, Cresswell T, Roberts C, Richards DP. Results of modified Latarjet reconstruction in patients with anteroinferior instability and significant bone loss. *Arthroscopy* 2007; **23**: 1033-1041 [PMID: 17916467 DOI: 10.1016/j.arthro.2007.08.009]
- 62 **Schmid SL**, Farshad M, Catanzaro S, Gerber C. The Latarjet procedure for the treatment of recurrence of anterior instability of the shoulder after operative repair: a retrospective case series of forty-nine consecutive patients. *J Bone Joint Surg Am* 2012; **94**: e75 [PMID: 22637215 DOI: 10.2106/JBJS.K.00380]
- 63 **Chen AL**, Hunt SA, Hawkins RJ, Zuckerman JD. Management of bone loss associated with recurrent anterior glenohumeral instability. *Am J Sports Med* 2005; **33**: 912-925 [PMID: 15933206 DOI: 10.1177/063546505277074]
- 64 **Lafosse L**, Boyle S. Arthroscopic Latarjet procedure. *J Shoulder Elbow Surg* 2010; **19**: 2-12 [PMID: 20188263 DOI: 10.1016/j.jse.2009.12.010]
- 65 **Boileau P**, Th  lu C  , Mercier N, Ohl X, Houghton-Clemmey R, Carles M, Trojani C. Arthroscopic Bristow-Latarjet combined with bankart repair restores shoulder stability in patients with glenoid bone loss. *Clin Orthop Relat Res* 2014; **472**: 2413-2424 [PMID: 24942959 DOI: 10.1007/s11999-014-3691-x]
- 66 **Provencher MT**, Bhatia S, Ghodadra NS, Grumet RC, Bach BR, Dewing CB, LeClere L, Romeo AA. Recurrent shoulder instability: current concepts for evaluation and management of glenoid bone loss. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 133-151 [PMID: 21123597 DOI: 10.2106/JBJS.J.00906]
- 67 **Warner JJ**, Gill TJ, O'hollerhan JD, Pathare N, Millett PJ. Anatomical glenoid reconstruction for recurrent anterior glenohumeral instability with glenoid deficiency using an autogenous tricortical iliac crest bone graft. *Am J Sports Med* 2006; **34**: 205-212 [PMID: 16303879 DOI: 10.1177/0363546505281798]
- 68 **Auffarth A**, Schauer J, Matis N, Kofler B, Hitzl W, Resch H. The J-bone graft for anatomical glenoid reconstruction in recurrent posttraumatic anterior shoulder dislocation. *Am J Sports Med* 2008; **36**: 638-647 [PMID: 18006673 DOI: 10.1177/0363546507309672]
- 69 **Scheibel M**, Nikulka C, Dick A, Schroeder RJ, Gerber Popp A, Haas NP. Autogenous bone grafting for chronic anteroinferior glenoid defects via a complete subscapularis tenotomy approach. *Arch Orthop Trauma Surg* 2008; **128**: 1317-1325 [PMID: 18196255 DOI: 10.1007/s00402-007-0560-z]
- 70 **Tokish JM**, Fitzpatrick K, Cook JB, Mallon WJ. Arthroscopic distal clavicular autograft for treating shoulder instability with glenoid bone loss. *Arthrosc Tech* 2014; **3**: e475-e481 [PMID: 25264509 DOI: 10.1016/j.eats.2014.05.006]
- 71 **Provencher MT**, Ghodadra N, LeClere L, Solomon DJ, Romeo AA. Anatomic osteochondral glenoid reconstruction for recurrent glenohumeral instability with glenoid deficiency using a distal tibia allograft. *Arthroscopy* 2009; **25**: 446-452 [PMID: 19341934 DOI: 10.1016/j.arthro.2008.10.017]
- 72 **Weng PW**, Shen HC, Lee HH, Wu SS, Lee CH. Open reconstruction of large bony glenoid erosion with allogeneic bone graft for recurrent anterior shoulder dislocation. *Am J Sports Med* 2009; **37**: 1792-1797 [PMID: 19483076 DOI: 10.1177/0363546509334590]
- 73 **Sayegh ET**, Mascarenhas R, Chalmers PN, Cole BJ, Verma NN, Romeo AA. Allograft reconstruction for glenoid bone loss in glenohumeral instability: a systematic review. *Arthroscopy* 2014; **30**: 1642-1649 [PMID: 24999006 DOI: 10.1016/j.arthro.2014.05.007]
- 74 **Kim SJ**, Kim SH, Park BK, Chun YM. Arthroscopic stabilization for recurrent shoulder instability with moderate glenoid bone defect in patients with moderate to low functional demand. *Arthroscopy* 2014; **30**: 921-927 [PMID: 24857422 DOI: 10.1016/j.arthro.2014.03.023]
- 75 **Mologne TS**, Provencher MT, Menzel KA, Vachon TA, Dewing CB. Arthroscopic stabilization in patients with an inverted pear glenoid: results in patients with bone loss of the anterior glenoid. *Am J Sports Med* 2007; **35**: 1276-1283 [PMID: 17387219 DOI: 10.1177/0363546507300262]
- 76 **Skendzel JG**, Sekiya JK. Diagnosis and management of humeral head bone loss in shoulder instability. *Am J Sports Med* 2012; **40**: 2633-2644 [PMID: 22343756 DOI: 10.1177/0363546512437314]
- 77 **Re P**, Gallo RA, Richmond JC. Transhumeral head plasty for large Hill-Sachs lesions. *Arthroscopy* 2006; **22**: 798.e1-798.e4 [PMID: 16848061]
- 78 **Kazel MD**, Sekiya JK, Greene JA, Bruker CT. Percutaneous correction (humeroplasty) of humeral head defects (Hill-Sachs) associated with anterior shoulder instability: a cadaveric study. *Arthroscopy* 2005; **21**: 1473-1478 [PMID: 16376238 DOI: 10.1016/j.arthro.2005.09.004]
- 79 **Purchase RJ**, Wolf EM, Hobgood ER, Pollock ME, Smalley CC. Hill-sachs "remplissage": an arthroscopic solution for the engaging hill-sachs lesion. *Arthroscopy* 2008; **24**: 723-726 [PMID: 18514117 DOI: 10.1016/j.arthro.2008.03.015]
- 80 **Sahajpal DT**, Zuckerman JD. Chronic glenohumeral dislocation. *J Am Acad Orthop Surg* 2008; **16**: 385-398 [PMID: 18611996]
- 81 **Zhu YM**, Lu Y, Zhang J, Shen JW, Jiang CY. Arthroscopic Bankart repair combined with remplissage technique for the treatment of anterior shoulder instability with engaging Hill-Sachs lesion: a report of 49 cases with a minimum 2-year follow-up. *Am J Sports Med* 2011; **39**: 1640-1647 [PMID: 21505080 DOI: 10.1177/0363546511400018]
- 82 **Boileau P**, O'Shea K, Vargas P, Pinedo M, Old J, Zumstein M. Anatomical and functional results after arthroscopic Hill-Sachs remplissage. *J Bone Joint Surg Am* 2012; **94**: 618-626 [PMID: 22488618 DOI: 10.2106/JBJS.K.00101]
- 83 **Longo UG**, Loppini M, Rizzello G, Ciuffreda M, Berton A, Maffulli N, Denaro V. Remplissage, humeral osteochondral grafts, weber osteotomy, and shoulder arthroplasty for the management of humeral bone defects in shoulder instability: systematic review and quantitative synthesis of the literature. *Arthroscopy* 2014; **30**: 1650-1666 [PMID: 25194166 DOI: 10.1016/j.arthro.2014.06.010]
- 84 **Weber BG**, Simpson LA, Hardegger F. Rotational humeral osteotomy for recurrent anterior dislocation of the shoulder associated with a large Hill-Sachs lesion. *J Bone Joint Surg Am* 1984; **66**: 1443-1450 [PMID: 6501339]
- 85 **Miniaci A**, Gish MW. Management of anterior glenohumeral instability associated with large Hill Sachs defects. *Tech Shoulder Elbow Surg* 2004; **5**: 170-175 [DOI: 10.1097/01.bte.0000137216.70574.ba]
- 86 **Miniaci A**, Martineau PA. Humeral head bony deficiency (large Hill Sachs). In: El Attrache NS, editor. Surgical techniques in sports medicine. Philadelphia: Lippincott, Williams and Wilkins, 2006
- 87 **Diklic ID**, Ganic ZD, Blagojevic ZD, Nho SJ, Romeo AA. Treatment of locked chronic posterior dislocation of the shoulder by reconstruction of the defect in the humeral head with an allograft. *J Bone Joint Surg Br* 2010; **92**: 71-76 [PMID: 20044682 DOI: 10.1302/0301-620X.92B1.22142]
- 88 **Copeland S**. The continuing development of shoulder replacement: "reaching the surface". *J Bone Joint Surg Am* 2006; **88**: 900-905 [PMID: 16595483 DOI: 10.2106/JBJS.F.00024]
- 89 **Raiss P**, Aldinger PR, Kasten P, Rickert M, Loew M. Humeral head resurfacing for fixed anterior glenohumeral dislocation. *Int Orthop* 2009; **33**: 451-456 [PMID: 18092162 DOI: 10.1007/s00264-007-0487-6]
- 90 **Gronidin P**, Leith J. Case series: Combined large Hill-Sachs and bony Bankart lesions treated by Latarjet and partial humeral head

- resurfacing: a report of 2 cases. *Can J Surg* 2009; **52**: 249-254 [PMID: 19503672]
- 91 **Moros C**, Ahmad CS. Partial humeral head resurfacing and Latarjet coracoid transfer for treatment of recurrent anterior glenohumeral instability. *Orthopedics* 2009; **32** [PMID: 19708626 DOI: 10.3928/01477447-20090624-21]
- 92 **Radnay CS**, Setter KJ, Chambers L, Levine WN, Bigliani LU, Ahmad CS. Total shoulder replacement compared with humeral head replacement for the treatment of primary glenohumeral osteoarthritis: a systematic review. *J Shoulder Elbow Surg* 2007; **16**: 396-402 [PMID: 17582789]
- 93 **Yamamoto N**, Itoi E, Abe H, Minagawa H, Seki N, Shimada Y, Okada K. Contact between the glenoid and the humeral head in abduction, external rotation, and horizontal extension: a new concept of glenoid track. *J Shoulder Elbow Surg* 2007; **16**: 649-656 [PMID: 17644006 DOI: 10.1016/j.jse.2006.12.012]
- 94 **Omori Y**, Yamamoto N, Koishi H. Measurement of the glenoid track in vivo, investigated by the three dimensional motion analysis using open MRI. Poster 502. Presented at the 57th Annual Meeting of the Orthopaedic Research Society; Long Beach, CA: 2011

P- Reviewer: Cui Q, Drosos GI, Emara K, Ko SH
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D



Medial ulnar collateral ligament reconstruction of the elbow in major league baseball players: Where do we stand?

Brandon J Erickson, Bernard R Bach Jr, Charles A Bush-Joseph, Nikhil N Verma, Anthony A Romeo

Brandon J Erickson, Bernard R Bach Jr, Charles A Bush-Joseph, Nikhil N Verma, Anthony A Romeo, Midwest Orthopaedics at Rush, Rush University Medical Center, Chicago, IL 60611, United States

Author contributions: Erickson BJ, Bach Jr BR, Bush-Joseph CA, Verma NN and Romeo AA designed this study, wrote and edited the manuscript.

Conflict-of-interest statement: No author has any conflicts of interest that pertain to the submitted article. Other conflicts of interest are listed in the document of conflict-of-interest statement.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Brandon J Erickson, MD, Midwest Orthopaedics at Rush, Rush University Medical Center, 1611 W Harrison St, Suite 300, Chicago, IL 60611, United States. brandon.j.erickson@gmail.com
 Telephone: +1-732-4925775
 Fax: +1-312-9422040

Received: January 25, 2016
 Peer-review started: January 25, 2016
 First decision: February 29, 2016
 Revised: March 8, 2016
 Accepted: March 24, 2016
 Article in press: March 25, 2016
 Published online: June 18, 2016

Abstract

The ulnar collateral ligament (UCL) is a vital structure to the overhead athlete, especially the baseball pitcher. For reasons not completely understood, UCL injuries

have become increasingly more common in major league baseball (MLB) pitchers over the past 10 years. UCL reconstruction (UCLR) is the current gold standard of treatment for these injuries in MLB pitchers who wish to return to sport (RTS) at a high level and who have failed a course of non-operative treatment. Results following UCLR in MLB pitchers have been encouraging, with multiple RTS rates now cited at greater than 80%. Unfortunately, with the rising number of UCLR, there has also been a spike in the number of revision UCLR in MLB pitchers. Similar to primary UCLR, the etiology of the increase in revision UCLR, aside from an increase in the number of pitchers who have undergone a primary UCLR, remains elusive. The current literature has attempted to address several questions including those surrounding surgical technique (method of exposure, graft choice, management of the ulnar nerve, concomitant elbow arthroscopy, *etc.*), post-operative rehabilitation strategies, and timing of RTS following UCLR. While some questions have been answered, many remain unknown. The literature surrounding UCLR in MLB pitchers will be reviewed, and future directions regarding this injury in these high level athletes will be discussed.

Key words: Ulnar collateral ligament; Ulnar collateral ligament reconstruction; Tommy John; Major league baseball; Pitcher; Baseball

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The number of ulnar collateral ligament (UCL) tears in major league baseball athletes is increasing with time. UCL reconstruction (UCLR) has become the gold standard for treatment of UCL tears. The outcomes of this surgery in elite level athletes is encouraging, with return to sport rates typically > 80%. Results following revision UCLR are less encouraging. Currently, there is no standardized rehabilitation protocol or timing to return to sport. Future research into graft choice,

surgical technique, management of the ulnar nerve, and rehabilitation protocols must be done to achieve the best possible results in this elite group of athletes.

Erickson BJ, Bach Jr BR, Bush-Joseph CA, Verma NN, Romeo AA. Medial ulnar collateral ligament reconstruction of the elbow in major league baseball players: Where do we stand? *World J Orthop* 2016; 7(6): 355-360 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/355.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.355>

INTRODUCTION

The ulnar collateral ligament (UCL) is one of the most important structures about the elbow in the overhead athlete, especially the baseball pitcher^[1,2]. While the UCL is not commonly stressed during activities of daily living, the baseball pitch imparts a significant amount of stress on the UCL, specifically the posterior band of the anterior bundle as it is this part of the UCL that sees the most stress at higher degrees of elbow flexion, causing the UCL to approach failure with each pitch^[3-5]. Without the secondary osseous and soft tissue restraints about the elbow, the UCL would fail after each pitch as the valgus force generated at the elbow with each pitch is approximately 64 nmol/L, while the ultimate load to failure of the native and reconstructed UCL is 34.29 nmol/L, and 30.55 nmol/L, respectively^[3].

Diagnosis of UCL tears is accomplished through patient history, physical exam maneuvers, and diagnostic imaging^[6]. Baseball pitchers who sustain tears to the UCL often report a decrease in velocity as well as a loss of accuracy in the time leading up to their injury^[7]. Some patients will have concomitant ulnar nerve symptoms, such as numbness/tingling of the pinky and ulnar half of the ring finger, weakness of the first dorsal interosseous muscle, and others. On physical exam, these patients can have pain along the course of the UCL. They may also have an increase in elbow valgus laxity compared to the contralateral arm, although this can be physiologic in baseball pitchers^[8]. Special physical exam maneuvers, including the moving valgus stress test and milking maneuver, are often positive in these patients as these tests stress the UCL in the position of throwing^[6,9,10]. Although anteroposterior, lateral, and external oblique radiographs are useful to rule out calcifications in the UCL as well as other pathology, magnetic resonance imaging (MRI) with or without arthrography is the current imaging modality of choice to diagnose a UCL tear^[11,12]. It seems that the increase in diagnosis of UCL tears is likely secondary to sports specialization in adolescents leading to an increase in the true number of UCL tears rather than an overdiagnosis on MRI like has been shown with superior labral tears^[13-15].

Should the UCL fail, the current gold standard treatment option for elite level overhead athletes who wish to return to sport (RTS) at a high level after failing non-

operative management is an UCL reconstruction (UCLR). Although repair of the UCL has been described with encouraging results for properly indicated adolescents, the results of repair have reproducibly been inferior to UCLR in major league baseball (MLB) athletes, and so UCLR has become to standard of care^[7,16,17]. UCLR was initially described by Jobe *et al.*^[18] in the literature in 1986, although the index surgery was performed on September 25, 1974 on then Los Angeles Dodgers pitcher, Tommy John.

The initial technique by Jobe *et al.*^[18] called for an elevation of the flexor pronator mass with a submuscular transposition of the ulnar nerve and a figure of eight graft configuration in which the graft was sutured to itself. Results of the initial Jobe technique demonstrated that greater than 60% of elite throwing athletes were able to RTS at their pre-surgical level of participation^[16]. However, 21% of these patients had a post-operative ulnar neuropraxia, all of which resolved by seven years^[16]. Following this initial description, concern arose over the treatment of the flexor pronator mass, as well as the routine submuscular transposition of the ulnar nerve. Therefore, since the initial description by Dr. Jobe, many modifications have been made to improve patient outcomes and decrease complications following UCLR; these modifications include a split in the flexor pronator mass, subcutaneous ulnar nerve transposition, and varying ways to secure the graft both on the ulna as well as humerus^[7,19-24].

EPIDEMIOLOGY OF UCLR IN MLB

Several studies have shown a recent increase in the number of UCL tears, and more specifically, the number of UCLR in MLB pitchers^[2,25-27]. Recent studies have also shown an increase in the number of UCLR performed in adolescent athletes, specifically those between the ages of 15-19 years^[28]. When evaluating MLB players, as expected, UCLR is significantly more common in MLB pitchers than any other position. When Conte *et al.*^[2] surveyed 5088 professional baseball players, there was a 16% prevalence of UCLR amongst pitchers compared to only 3% amongst all other position players. Interestingly, this survey study by Conte *et al.*^[2] found that 25% of all MLB pitchers admitted to a history of UCLR, while 15% of minor league pitchers had undergone UCLR. No difference was seen in the prevalence of UCLR between pitchers born in the United States vs those born in Latin America countries^[2]. Erickson *et al.*^[25,26] showed a significant increase in the number of UCLR in MLB pitchers from 2000 to 2012 ($P = 0.014$), and further studies have demonstrated that the number has continued to rise in 2013 and 2014^[2]. Interestingly, there was no statistically significant increase in the number of UCLR in MLB pitchers between the 1980s and 1990s^[25]. MLB pitchers who underwent primary UCLR played an average of 5.27 ± 4.34 seasons prior to surgery^[25]. Furthermore, pitchers who grew up in warm weather climates were more likely to undergo UCLR earlier in their MLB career than

those from cold weather climates^[26]. While the increase in UCLR has been clearly documented, the reason for this increase remains unknown. There have been no prospective studies in the literature to date that have definitively shown what the cause of this increase in the number of UCLR is.

Several studies have, however, demonstrated risk factors for elbow injuries in adolescent athletes including pitching more than 100 innings per year, high pitch counts, pitching on consecutive days, pitching for multiple teams, pitching while fatigued, pitching year round, pitching with higher velocity, pitching with supraspinatus weakness, geography, pitching with a glenohumeral internal rotation deficit, and most recently pitching with a loss of total arc of motion, especially decreased external rotation^[26,29-38]. While these risk factors have been well established, there have been no studies to date that have been able to show a risk reduction in the number of UCLR by implementing programs to limit these risk factors. This is an area that requires further attention in the coming years as there does not appear to be an end in sight to the growing number of UCLR, and injury prevention must be at the forefront of current research to protect both MLB and adolescent pitchers^[39].

Although the increase in the number of primary UCLR in MLB pitchers is worrisome, a more pressing concern is the increase in the number of revision UCLR in these athletes^[2,40-42]. Wilson *et al.*^[42] evaluated 271 professional baseball pitchers who underwent primary UCLR and found that 40 (15%) required at least one revision UCLR during their pitching career while three pitchers required a second revision. The revision surgery occurred an average of 5.2 ± 3.2 years following the index UCLR, although there was a wide range from 1-13 years. As pitchers are beginning to undergo UCLR at earlier ages, it begs the question if the longevity of these athletes is going to decrease with time. Some would argue that a pitcher has a finite number of innings he can throw. If adolescent athletes are throwing year round and not following the rules set forth for their protection regarding inning and pitch count limits, these athletes could begin to undergo their index UCLR at earlier ages, causing the likelihood of a revision UCLR to rise, thereby limiting the ultimate number of years they can pitch in MLB.

OUTCOMES FOLLOWING PRIMARY AND REVISION UCLR IN MLB PITCHERS

Primary

There have been many studies that have looked at publically available data to determine the outcomes following UCLR in MLB pitchers as it relates to RTS as well as overall performance upon RTS^[25,43]. Erickson *et al.*^[25] evaluated all MLB pitchers from 1974 to 2012 who underwent UCLR using publically available data, team injury reports, *etc.*, and compared this group to a matched control group of healthy MLB pitchers. The authors found a total of 179 pitchers who underwent

UCLR having pitched at least one game in MLB. Of these 179 pitchers, 148 (83%) were able to RTS and pitch in at least one MLB game following UCLR, 174 (97.2%) were able to RTS in either the major or minor leagues, and only 5 pitchers (2.8%) were unable to pitch again in the major or minor leagues. The pitchers were able to RTS at an average of 20.5 ± 9.72 mo following their UCLR and pitched for an average of 3.9 ± 2.84 years after their RTS. The number of years pitched after RTS may have been falsely low as 56 of these pitchers were still active in MLB at the time the study was conducted.

When the authors evaluated the performance of these MLB pitchers upon RTS they found that pitchers pitched fewer innings in season following their UCLR and had fewer wins and losses per season compared to before surgery^[25]. Furthermore, pitchers had a significantly lower earned run average (ERA) and walks plus hits per inning pitched (WHIP) following surgery than beforehand. WHIP is a sabermetric that is calculated by summing a pitcher's total walks and hits for one season and dividing the sum by the number of innings pitched that season. A later study conducted by Jiang *et al.*^[43] evaluated 28 MLB pitchers between 2008-2010 who underwent UCLR to determine if pitching velocity, as well as performance variables changed compared both to pre-operative levels upon RTS in MLB as well as control group of healthy MLB pitchers. The authors found a statistically significant decrease in mean pitch velocity of both the fastball and changeup in each post-injury year compared to pre-injury velocities. The average decrease in fastball velocity for post-UCLR years 1-3 was 1.3, 1.0, 1.0 miles per hour (mph) respectively. The average decrease in changeup velocity for post-UCLR years 1-3 was 1.2, 1.3, 1.0 mph respectively. Furthermore, a decrease in curveball velocity was seen in post UCLR years 2 and 3 that averaged 1.0 and 1.7 mph respectively. However, despite these differences between pre and post UCLR pitching velocities in the group of pitchers who underwent UCLR, there was no significant difference in mean pitch velocity for any pitch, in any year following UCLR in cases vs matched controls^[43]. Hence, this could mean that pitchers who sustain UCL tears and undergo UCLR are throwing faster than their peers at baseline. Lansdown *et al.*^[44] performed a similar study and found similar results; pitchers who underwent UCLR had a significant decrease in mean fastball velocity (91.3 mph vs 90.6 mph) ($P = 0.003$), with the greatest decrease in velocity seen in pitchers older than 35 years of age (91.7 to 88.8 mph) ($P = 0.0048$). Despite the belief from players, parents, and coaches as shown by Ahmad *et al.*^[45] that UCLR will improve a pitchers velocity, these two studies clearly demonstrate a small but significant decrease in velocity following UCLR.

Revision

While the results following primary UCLR in MLB pitchers are reliable, the results following revision UCLR in the same patient population are not as encouraging^[40]. Marshall *et al.*^[40] evaluated 33 MLB pitchers who under-

went revision UCLR and compared these pitchers to matched controls to determine if differences existed in performance upon RTS. The authors found that 65.5% of pitchers who underwent revision UCLR were able to return to RTS in MLB while 84.8% were able to RTS in either the major or minor leagues; both rates are lower than RTS rates following index UCLR of 83% for MLB and 97.2% for either major or minor leagues^[25]. Interestingly, when Liu *et al*^[46] also evaluated 31 MLB pitchers following revision UCLR surgery, the authors found that while 65% were able to RTS in the MLB for one game or more, only 42.8% were able to pitch 10 or more games in MLB. Similar to the reported length of recovery following primary UCLR of 20.5 mo, the average time to RTS following revision UCLR was 20.76 mo^[25,46].

When compared to pre-injury performance levels, following revision UCLR pitchers pitched fewer innings, had fewer wins and losses, and let up more walks per nine innings. The only performance parameter that improved was the number of runs allowed per nine innings declined following revision surgery. Furthermore, pitchers who were able to RTS following revision UCLR pitched significantly fewer seasons than matched controls (2.6 vs 4.9 seasons)^[46]. Following revision UCLR, pitchers had no difference in ERA and WHIP when compared to controls^[40]. Unfortunately, following revision UCLR pitchers threw significantly fewer innings, gave up significantly more walks, and had significantly fewer wins (although they also had significantly fewer losses) compared to controls^[40].

FUTURE DIRECTIONS

Although there have been numerous studies that have reported on the RTS rate and outcomes of MLB pitchers following both primary and revision UCLR, there have been no prospective studies in this athlete cohort that have evaluated RTS rate or success upon RTS as it relates to surgical technique, graft choice, management of the ulnar nerve, concomitant arthroscopy, rehabilitation protocol, and timing of RTS^[25,40,44,46]. In order to improve outcomes, it is necessary to determine if these variables influence outcomes in MLB pitchers. One topic that has received recent attention is when to allow pitchers to throw for the first time following UCLR. While some protocols wait five months or more, some allow throwing as early as three to four months. Unfortunately, no data exists on the ideal timing, so these protocols have not yet been standardized to efficiently and safely return these pitchers to sport.

Furthermore, large, prospective studies must be designed to follow elite pitchers starting at the Little League level through their career. Although only a small percentage of these athletes will become MLB pitchers, it would be extremely valuable to see if implementing some of the rules and regulations aimed at decreasing elbow injuries were effective, and likewise to see if pitchers who did not adhere to the regulations were at higher risk for undergoing UCLR later in life. This would

also give the orthopaedic community an idea if pitchers do in deed have a finite number of innings their body will allow them to pitch, thereby proving to coaches and parents the importance of limiting excessive pitching at early ages.

CONCLUSION

Recent times have seen an increase in the number of UCLR in MLB pitchers. While evidence has shown a greater than 80% RTS rate following UCLR, the RTS rate following revision UCLR is not as high. Further large scale, prospective studies are necessary to help dictate treatment algorithms in these high level athletes.

REFERENCES

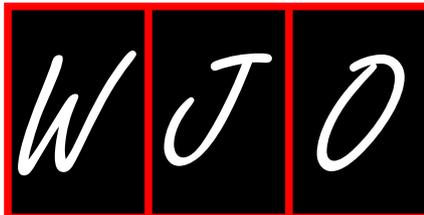
- 1 **Morrey BF**. Applied anatomy and biomechanics of the elbow joint. *Instr Course Lect* 1986; **35**: 59-68 [PMID: 3819430]
- 2 **Conte SA**, Fleisig GS, Dines JS, Wilk KE, Aune KT, Patterson-Flynn N, ElAttrache N. Prevalence of Ulnar Collateral Ligament Surgery in Professional Baseball Players. *Am J Sports Med* 2015; **43**: 1764-1769 [PMID: 25925603 DOI: 10.1177/0363546515580792]
- 3 **Morrey BF**, An KN. Articular and ligamentous contributions to the stability of the elbow joint. *Am J Sports Med* 1983; **11**: 315-319 [PMID: 6638246 DOI: 10.1177/036354658301100506]
- 4 **Munshi M**, Pretterklieber ML, Chung CB, Haghghi P, Cho JH, Trudell DJ, Resnick D. Anterior bundle of ulnar collateral ligament: evaluation of anatomic relationships by using MR imaging, MR arthrography, and gross anatomic and histologic analysis. *Radiology* 2004; **231**: 797-803 [PMID: 15105452 DOI: 10.1148/radiol.2313030560]
- 5 **Dugas JR**, Ostrander RV, Cain EL, Kingsley D, Andrews JR. Anatomy of the anterior bundle of the ulnar collateral ligament. *J Shoulder Elbow Surg* 2007; **16**: 657-660 [PMID: 17583541 DOI: 10.1016/j.jse.2006.11.009]
- 6 **Erickson BJ**, Harris JD, Chalmers PN, Bach BR, Verma NN, Bush-Joseph CA, Romeo AA. Ulnar Collateral Ligament Reconstruction: Anatomy, Indications, Techniques, and Outcomes. *Sports Health* 2015; **7**: 511-517 [PMID: 26502444 DOI: 10.1177/1941738115607208]
- 7 **Cain EL**, Andrews JR, Dugas JR, Wilk KE, McMichael CS, Walter JC, Riley RS, Arthur ST. Outcome of ulnar collateral ligament reconstruction of the elbow in 1281 athletes: Results in 743 athletes with minimum 2-year follow-up. *Am J Sports Med* 2010; **38**: 2426-2434 [PMID: 20929932 DOI: 10.1177/0363546510378100]
- 8 **Ciccotti MG**, Atanda A, Nazarian LN, Dodson CC, Holmes L, Cohen SB. Stress sonography of the ulnar collateral ligament of the elbow in professional baseball pitchers: a 10-year study. *Am J Sports Med* 2014; **42**: 544-551 [PMID: 24473498 DOI: 10.1177/0363546513516592]
- 9 **Erickson BJ**, Bach BR, Cohen MS, Bush-Joseph CA, Cole BJ, Verma NN, Nicholson GP, Romeo AA. Ulnar Collateral Ligament Reconstruction: The Rush Experience. *Orthop J Sports Med* 2016; **4**: 2325967115626876 [PMID: 26862538 DOI: 10.1177/2325967115626876]
- 10 **Cain EL**, Dugas JR, Wolf RS, Andrews JR. Elbow injuries in throwing athletes: a current concepts review. *Am J Sports Med* 1985; **31**: 621-635 [PMID: 12860556]
- 11 **Magee T**. Accuracy of 3-T MR arthrography versus conventional 3-T MRI of elbow tendons and ligaments compared with surgery. *AJR Am J Roentgenol* 2015; **204**: W70-W75 [PMID: 25539278 DOI: 10.2214/AJR.14.12553]
- 12 **Podesta L**, Crow SA, Volkmer D, Bert T, Yocum LA. Treatment of partial ulnar collateral ligament tears in the elbow with platelet-rich plasma. *Am J Sports Med* 2013; **41**: 1689-1694 [PMID: 23666850]

- DOI: 10.1177/0363546513487979]
- 13 **Sheridan K**, Kreulen C, Kim S, Mak W, Lewis K, Marder R. Accuracy of magnetic resonance imaging to diagnose superior labrum anterior-posterior tears. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2645-2650 [PMID: 24985524 DOI: 10.1007/s00167-014-3109-z]
 - 14 **Myer GD**, Jayanthi N, DiFiori JP, Faigenbaum AD, Kiefer AW, Legerstedt D, Micheli LJ. Sport Specialization, Part I: Does Early Sports Specialization Increase Negative Outcomes and Reduce the Opportunity for Success in Young Athletes? *Sports Health* 2015; **7**: 437-442 [PMID: 26502420 DOI: 10.1177/1941738115598747]
 - 15 **Myer GD**, Jayanthi N, DiFiori JP, Faigenbaum AD, Kiefer AW, Legerstedt D, Micheli LJ. Sports Specialization, Part II: Alternative Solutions to Early Sport Specialization in Youth Athletes. *Sports Health* 2016; **8**: 65-73 [PMID: 26517937 DOI: 10.1177/1941738115614811]
 - 16 **Conway JE**, Jobe FW, Glousman RE, Pink M. Medial instability of the elbow in throwing athletes. Treatment by repair or reconstruction of the ulnar collateral ligament. *J Bone Joint Surg Am* 1992; **74**: 67-83 [PMID: 1734015]
 - 17 **Savoie FH**, Trenhaile SW, Roberts J, Field LD, Ramsey JR. Primary repair of ulnar collateral ligament injuries of the elbow in young athletes: a case series of injuries to the proximal and distal ends of the ligament. *Am J Sports Med* 2008; **36**: 1066-1072 [PMID: 18443280 DOI: 10.1177/0363546508315201]
 - 18 **Jobe FW**, Stark H, Lombardo SJ. Reconstruction of the ulnar collateral ligament in athletes. *J Bone Joint Surg Am* 1986; **68**: 1158-1163 [PMID: 3771597]
 - 19 **Vitale MA**, Ahmad CS. The outcome of elbow ulnar collateral ligament reconstruction in overhead athletes: a systematic review. *Am J Sports Med* 2008; **36**: 1193-1205 [PMID: 18490476 DOI: 10.1177/0363546508319053]
 - 20 **Erickson BJ**, Chalmers PN, Bush-Joseph CA, Verma NN, Romeo AA. Ulnar Collateral Ligament Reconstruction of the Elbow: A Systematic Review of the Literature. *Orthop J Sports Med* 2015; **3**: 2325967115618914 [PMID: 26740956 DOI: 10.1177/2325967115618914]
 - 21 **Rohrbough JT**, Altchek DW, Hyman J, Williams RJ, Botts JD. Medial collateral ligament reconstruction of the elbow using the docking technique. *Am J Sports Med* 2002; **30**: 541-548 [PMID: 12130409]
 - 22 **Dines JS**, ElAttrache NS, Conway JE, Smith W, Ahmad CS. Clinical outcomes of the DANE TJ technique to treat ulnar collateral ligament insufficiency of the elbow. *Am J Sports Med* 2007; **35**: 2039-2044 [PMID: 17703003 DOI: 10.1177/0363546507305802]
 - 23 **Morgan RJ**, Starman JS, Habet NA, Peindl RD, Bankston LS, D'Alessandro DD, Connor PM, Fleischli JE. A biomechanical evaluation of ulnar collateral ligament reconstruction using a novel technique for ulnar-sided fixation. *Am J Sports Med* 2010; **38**: 1448-1455 [PMID: 20442324 DOI: 10.1177/0363546510363463]
 - 24 **Andrews JR**, Timmerman LA. Outcome of elbow surgery in professional baseball players. *Am J Sports Med* 1995; **23**: 407-413 [PMID: 7573648]
 - 25 **Erickson BJ**, Gupta AK, Harris JD, Bush-Joseph C, Bach BR, Abrams GD, San Juan AM, Cole BJ, Romeo AA. Rate of return to pitching and performance after Tommy John surgery in Major League Baseball pitchers. *Am J Sports Med* 2014; **42**: 536-543 [PMID: 24352622 DOI: 10.1177/0363546513510890]
 - 26 **Erickson BJ**, Harris JD, Tetreault M, Bush-Joseph C, Cohen M, Romeo AA. Is Tommy John Surgery Performed More Frequently in Major League Baseball Pitchers From Warm Weather Areas? *Orthop J Sports Med* 2014; **2**: 2325967114553916 [PMID: 26535277 DOI: 10.1177/2325967114553916]
 - 27 **Osbahr DC**, Cain EL, Raines BT, Fortenbaugh D, Dugas JR, Andrews JR. Long-term Outcomes After Ulnar Collateral Ligament Reconstruction in Competitive Baseball Players: Minimum 10-Year Follow-up. *Am J Sports Med* 2014; **42**: 1333-1342 [PMID: 24705899 DOI: 10.1177/0363546514528870]
 - 28 **Erickson BJ**, Nwachukwu BU, Rosas S, Schairer WW, McCormick FM, Bach BR, Bush-Joseph CA, Romeo AA. Trends in Medial Ulnar Collateral Ligament Reconstruction in the United States: A Retrospective Review of a Large Private-Payer Database From 2007 to 2011. *Am J Sports Med* 2015; **43**: 1770-1774 [PMID: 26129959 DOI: 10.1177/0363546515580304]
 - 29 **Anz AW**, Bushnell BD, Griffin LP, Noonan TJ, Torry MR, Hawkins RJ. Correlation of torque and elbow injury in professional baseball pitchers. *Am J Sports Med* 2010; **38**: 1368-1374 [PMID: 20400752 DOI: 10.1177/0363546510363402]
 - 30 **Bushnell BD**, Anz AW, Noonan TJ, Torry MR, Hawkins RJ. Association of maximum pitch velocity and elbow injury in professional baseball pitchers. *Am J Sports Med* 2010; **38**: 728-732 [PMID: 20093420 DOI: 10.1177/0363546509350067]
 - 31 **Byram IR**, Bushnell BD, Dugger K, Charron K, Harrell FE, Noonan TJ. Preseason shoulder strength measurements in professional baseball pitchers: identifying players at risk for injury. *Am J Sports Med* 2010; **38**: 1375-1382 [PMID: 20489215 DOI: 10.1177/0363546509360404]
 - 32 **Dines JS**, Frank JB, Akerman M, Yocum LA. Glenohumeral internal rotation deficits in baseball players with ulnar collateral ligament insufficiency. *Am J Sports Med* 2009; **37**: 566-570 [PMID: 19059890 DOI: 10.1177/0363546508326712]
 - 33 **Fleisig GS**, Andrews JR, Cutter GR, Weber A, Loftice J, McMichael C, Hassell N, Lyman S. Risk of serious injury for young baseball pitchers: a 10-year prospective study. *Am J Sports Med* 2011; **39**: 253-257 [PMID: 21098816 DOI: 10.1177/0363546510384224]
 - 34 **Lyman S**, Fleisig GS, Andrews JR, Osinski ED. Effect of pitch type, pitch count, and pitching mechanics on risk of elbow and shoulder pain in youth baseball pitchers. *Am J Sports Med* 2002; **30**: 463-468 [PMID: 12130397]
 - 35 **Petty DH**, Andrews JR, Fleisig GS, Cain EL. Ulnar collateral ligament reconstruction in high school baseball players: clinical results and injury risk factors. *Am J Sports Med* 2004; **32**: 1158-1164 [PMID: 15262637 DOI: 10.1177/0363546503262166]
 - 36 **Wilk KE**, Macrina LC, Fleisig GS, Aune KT, Porterfield RA, Harker P, Evans TJ, Andrews JR. Deficits in Glenohumeral Passive Range of Motion Increase Risk of Shoulder Injury in Professional Baseball Pitchers: A Prospective Study. *Am J Sports Med* 2015; **43**: 2379-2385 [PMID: 26272516 DOI: 10.1177/0363546515594380]
 - 37 **Wilk KE**, Macrina LC, Fleisig GS, Aune KT, Porterfield RA, Harker P, Evans TJ, Andrews JR. Deficits in glenohumeral passive range of motion increase risk of elbow injury in professional baseball pitchers: a prospective study. *Am J Sports Med* 2014; **42**: 2075-2081 [PMID: 24944295 DOI: 10.1177/0363546514538391]
 - 38 **Yang J**, Mann BJ, Guettler JH, Dugas JR, Irrgang JJ, Fleisig GS, Albright JP. Risk-Prone Pitching Activities and Injuries in Youth Baseball: Findings From a National Sample. *Am J Sports Med* 2014; **42**: 1456-1463 [PMID: 24627578 DOI: 10.1177/0363546514524699]
 - 39 **Erickson BJ**. The epidemic of Tommy John surgery: the role of the orthopedic surgeon. *Am J Orthop (Belle Mead NJ)* 2015; **44**: E36-E37 [PMID: 25566564]
 - 40 **Marshall NE**, Keller RA, Lynch JR, Bey MJ, Moutzouros V. Pitching performance and longevity after revision ulnar collateral ligament reconstruction in Major League Baseball pitchers. *Am J Sports Med* 2015; **43**: 1051-1056 [PMID: 25862037 DOI: 10.1177/0363546515579636]
 - 41 **Dines JS**, Yocum LA, Frank JB, ElAttrache NS, Gambardella RA, Jobe FW. Revision surgery for failed elbow medial collateral ligament reconstruction. *Am J Sports Med* 2008; **36**: 1061-1065 [PMID: 18443277 DOI: 10.1177/0363546508314796]
 - 42 **Wilson AT**, Pidgeon TS, Morrell NT, DaSilva MF. Trends in Revision Elbow Ulnar Collateral Ligament Reconstruction in Professional Baseball Pitchers. *J Hand Surg Am* 2015; **40**: 2249-2254 [PMID: 26328904 DOI: 10.1016/j.jhsa.2015.07.024]
 - 43 **Jiang JJ**, Leland JM. Analysis of pitching velocity in major league baseball players before and after ulnar collateral ligament reconstruction. *Am J Sports Med* 2014; **42**: 880-885 [PMID: 24496506 DOI: 10.1177/0363546513519072]
 - 44 **Lansdown DA**, Feeley BT. The Effect of Ulnar Collateral Ligament

- Reconstruction on Pitch Velocity in Major League Baseball Pitchers. *Orthop J Sports Med* 2014; **2**: 2325967114522592 [PMID: 26535301 DOI: 10.1177/2325967114522592]
- 45 **Ahmad CS**, Grantham WJ, Greiwe RM. Public perceptions of Tommy John surgery. *Phys Sportsmed* 2012; **40**: 64-72 [PMID: 22759607 DOI: 10.3810/psm.2012.05.1966]
- 46 **Liu JN**, Garcia GH, Conte S, ElAttrache N, Altchek DW, Dines JS. Outcomes in revision Tommy John surgery in Major League Baseball pitchers. *J Shoulder Elbow Surg* 2016; **25**: 90-97 [PMID: 26687472 DOI: 10.1016/j.jse.2015.08.040]

P- Reviewer: Angoules A, Guerado E, Metzger PD
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Li D





Antimicrobial technology in orthopedic and spinal implants

Adam EM Eltorai, Jack Haglin, Sudheesha Perera, Bielinsky A Brea, Roy Ruttiman, Dioscaris R Garcia, Christopher T Born, Alan H Daniels

Adam EM Eltorai, Sudheesha Perera, Roy Ruttiman, Warren Alpert Medical School, Brown University, Providence, RI 02906, United States

Jack Haglin, Department of Biology, Brown University, Providence, RI 02906, United States

Bielinsky A Brea, Center for Biomedical Engineering, Brown University, Providence, RI 02906, United States

Dioscaris R Garcia, Christopher T Born, Alan H Daniels, Department of Orthopaedic Surgery, Warren Alpert Medical School, Brown University, Providence, RI 02906, United States

Author contributions: All the authors contributed to the conception and design of the work, revised carefully the content and approved the final version of the manuscript writing.

Conflict-of-interest statement: Dioscaris R Garcia: Materials Science Associates: Paid consultant. Christopher T Born: Biointraface: Stock or stock Options; Unpaid consultant; Illuminoss: Paid consultant; Stock or stock Options; Stryker: Paid consultant; Research support. Alan H Daniels: DePuy, A Johnson and Johnson Company: Other financial or material support; Paid consultant; Globus Medical: Paid consultant; Medtronic Sofamor Danek: Other financial or material support; Orthofix, Inc.: Research support; Osseus: Unpaid consultant; Stryker: Other financial or material support; Paid consultant. The other authors have no conflicts of interest. There is no conflict of interest associated with the senior author or coauthors who contributed their efforts to this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Alan H Daniels, MD, Assistant Professor, Department of Orthopedic Surgery, Warren Alpert Medical School, Brown University, 100 Butler Drive, Providence, RI 02906, United States. alan_daniels@brown.edu

Telephone: +1-401-3301420
Fax: +1-401-3301495

Received: February 3, 2016
Peer-review started: February 14, 2016
First decision: March 21, 2016
Revised: April 6, 2016
Accepted: April 21, 2016
Article in press: April 22, 2016
Published online: June 18, 2016

Abstract

Infections can hinder orthopedic implant function and retention. Current implant-based antimicrobial strategies largely utilize coating-based approaches in order to reduce biofilm formation and bacterial adhesion. Several emerging antimicrobial technologies that integrate a multidisciplinary combination of drug delivery systems, material science, immunology, and polymer chemistry are in development and early clinical use. This review outlines orthopedic implant antimicrobial technology, its current applications and supporting evidence, and clinically promising future directions.

Key words: Antimicrobial; Coated implants; Antibiotic; Antiseptic; Nano-silver; Photoactive

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Infections can hinder orthopedic implant function and retention. Current implant-based antimicrobial strategies largely utilize coating-based approaches in order to reduce biofilm formation and bacterial adhesion. Several emerging antimicrobial technologies that integrate a multidisciplinary combination of drug delivery systems, material science, immunology, and polymer chemistry are in development and early clinical use. This review outlines the latest orthopedic implant antimicrobial technologies-including updates on chitosan

coatings, photoactive-based coatings, electrospinning technology, integrated biofilms-highlighting the current applications, supporting evidence, and clinically-promising future directions.

Eltorai AEM, Haglin J, Perera S, Brea BA, Ruttiman R, Garcia DR, Born CT, Daniels AH. Antimicrobial technology in orthopedic and spinal implants. *World J Orthop* 2016; 7(6): 361-369 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/361.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.361>

BACKGROUND

Orthopedic implants are commonly used in spine surgery, arthroplasty, arthrodesis, as well for applications in treating fractures and nonunions^[1]. Typically formulated from titanium, stainless steel, cobalt-chromium, or polyethylene polymers, orthopedic implants can serve as niduses for infection and may hinder infection clearance due to biofilm formation on the implant surface^[2]. Orthopedic implant-associated infections are challenging complications which can lead to delayed healing, implant loosening, implant removal, amputation, or even death^[3].

In many infections, bacteria will form a biofilm on the implant, increasing their resistance to antibiotics and resulting in infection persistence despite aggressive surgical debridement and prolonged antibiotic treatments^[4,5]. A biofilm is an aggregated mass of bacteria that can form on the surface of an orthopedic implant, providing the ideal environment for bacteria to flourish. Such bacterial growths are difficult to eliminate and present a serious challenge in implant development^[6,7]. In the United States, orthopedic implants are associated with an approximate 5% infection rate, representing 100000 infections per year^[8]. This frequency represents a notable economic burden on both patients and health care providers. Although exact figures are elusive, even with the existence of antibiotic prophylactic it is estimated that implant infections increase the overall cost of hospitalization up to 45% on average^[9,10].

ANTIMICROBIAL COATED IMPLANTS

Current antimicrobial strategies have largely focused on coating-based approaches-each of which aims to prevent infection by mitigating biofilm formation^[11]. Key coatings include antibiotic, antiseptic, nano-silver, and photoactive-based coatings^[11].

Antibiotic-based coatings

Antibiotic coatings allow for local delivery of antibiotics with a sustained release based on the drug carrier pharmacokinetics^[12]. While various antibiotics have been studied (*e.g.*, amoxicillin, vancomycin, cephalothin, and tobramycin), the most widely studied antibiotic for such coatings has been gentamicin^[11]. Common

biocompatible drug carriers for the coatings include polymethylmethacrylate (PMMA), poly(lactic-co-glycolic acid) (PLGA), poly(lactic acid), polyethylene glycol, and poly(D,L)lactide (Figure 1)^[7]. Hydroxyapatite (HA) was recently shown to be an effective drug carrier of gentamicin^[13,14].

Neut *et al*^[15] demonstrated the wide-spectrum antibacterial efficacy of a gentamicin coating *in vitro* through investigating infection prophylaxis of *Staphylococcus aureus* (*S. aureus*) in cementless total-hip arthroplasty. In a rabbit model, Alt *et al*^[16] found that the gentamicin-HA composite provided a statistically significant reduction in infection rate when compared to uncoated total joint replacements. In patient trials, gentamicin-coated implants have displayed promising preliminary results (Figure 1)^[17-20]. Limitations of antibiotic coatings include the use of fixed, predetermined antibiotics; limited duration of drug elution; and the risk of developing drug resistance^[21].

To overcome the limited duration of drug elution, Ambrose *et al*^[22-24] developed antibiotic-impregnated bioresorbable microspheres for sustained release of antibiotics over several weeks-which have been shown to reduce infection rates in animal models. Antiseptic-based coatings have emerged to address antibiotic coatings fixed bactericidal spectrum and possible drug resistance limitations. Antibiotic-based coatings are currently the most commonly utilized local antimicrobial clinical delivery method due to the well characterized nature of the antimicrobial agents. These coatings are limited by antibiotic classes, which are compatible with the chemistry of the coating matrix. Besides from pharmacokinetic limitations, antibiotic-based coatings represent the most accepted antimicrobial option available.

Antiseptic-based coatings

In contrast to antibiotic coatings, which are formulated to work against specific bacterial strains, antiseptic-based coatings are intended to combat a wide range of bacteria by way of more general chemical agents. For this reason antiseptic coatings are less likely to induce bacterial resistance compared to antibiotics^[25,26]. Common antiseptics include chlorhexidine and chloroxylenol, which are thought to act through the interaction of their natural cationic nature with the anionic phosphate residue of the lipid molecules in bacterial cell membranes. This ionic adsorption damages cell membranes and limits bacterial adhesion (Figure 2)^[27,28]. In 1998, Darouiche^[8] first demonstrated the effectiveness of antiseptic coatings on titanium cylinders studied *in vitro* with human serum before DeJong *et al*^[29] tested chlorhexidine and chloroxylenol in a goat model, finding that these two antiseptics reduced external fixator pin tract infections. Ho *et al*^[30] demonstrated *in vivo* efficacy of antiseptic coatings in humans by reducing vascular and epidural catheter infection with application of a chlorhexidine-impregnated dressing. Due to their broad spectrum efficacy, antiseptic-based coatings are not without some level of generalized toxicity. Because of their general toxicity, antiseptic based

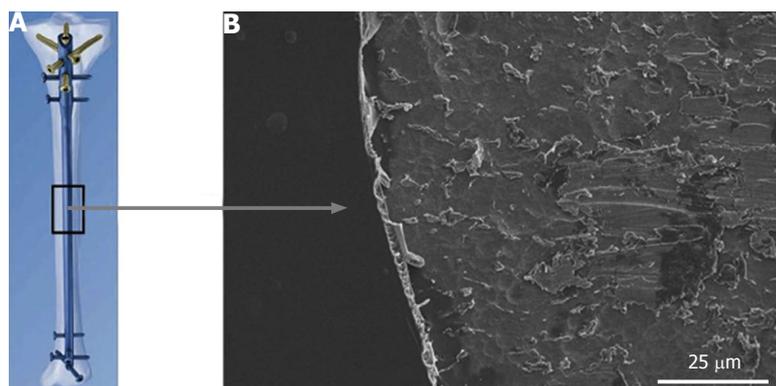


Figure 1 Diagram of tibial nail with gentamicin coating (A), visualized on metal implant using scanning electron microscopy (B)^[20].

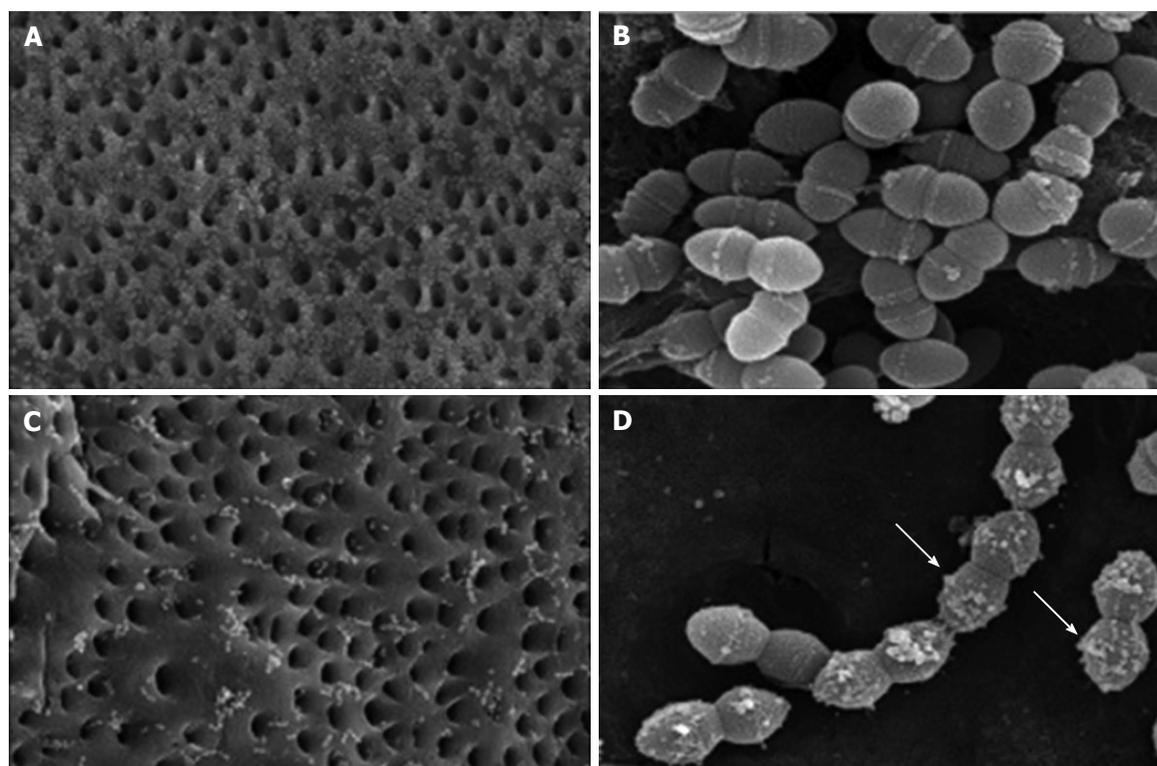


Figure 2 Scanning electron microscopy images of *Enterococcus faecalis*-infected dentin blocks treated with saline and chlorhexidine. Blocks treated with saline solution for 10 min show many adhering *Enterococcus faecalis* (A, × 1500) with normal shape (B, × 20000). The group soaked with 2% chlorhexidine shows fewer adhering bacteria (C, × 1500) and chlorhexidine particles attached to bacterial membranes (D, × 20000, white arrows)^[26].

coatings are more commonly utilized as topical dressings.

Chitosan coatings

Chitosan is a polymer of chitin that exhibits active antimicrobial properties. Recent pre-clinical studies have provided evidence that several composites of chitosan may act as effective antimicrobial agents suited for titanium orthopedic implants. Yang *et al.*^[31] tested a vancomycin-chitosan composite by monitoring the proliferation of human osteoblast cells *in vitro* using methyl thiazole tetrazolium and cell adhesion using FEMSEM. They found that vancomycin-chitosan coated implants displayed lesser biofilm formation, a result corroborated by *in vivo* experiments in a rabbit model^[31].

In fact, some results indicate that a simple mixtures of 2%-3% chitosan and 2% cinnamon oil may also hold antimicrobial properties against *Staphylococcus epidermidis* (*S. epidermidis*) on titanium implants^[32]. Most recently, Qin *et al.*^[33] revealed preliminary *in vitro* results suggesting that chitosan-casein phosphopeptides coatings could provide antimicrobial benefits for cobalt matrix orthopedic implants. Other studies have suggested that chitosan alone may not be sufficiently potent as an antimicrobial agent and suffers from poor release kinetics. More current studies have focused on the synergistic use of chitosan and antibacterial agents with more promising results. As yet we are not aware of any clinical trials incorporating chitosan-based coats.

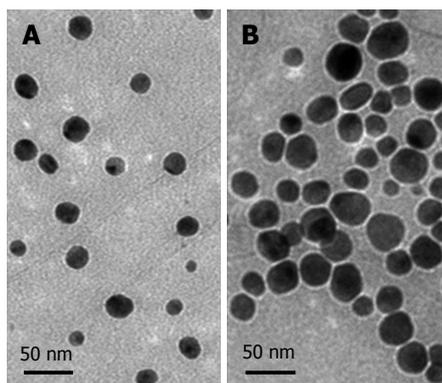


Figure 3 Silver nanoparticles of two sizes: Small (A) and Large (B), visualized via transmission electron microscopy^[42].

Nano-silver coatings

The antimicrobial properties of silver particles are well-established^[34-38]. Silver particles have several known mechanisms of action including binding to thiol groups of enzymes, cell membranes, and nucleic acids, resulting in structural abnormalities, a damaged cell envelope, and inhibition of cell division^[39-41]. Silver nanoparticles (Figure 3)^[42] are typically incorporated into titanium surfaces or polymeric coating to control the release rate and duration of the bioactive silver^[11,43-45]. Electrical currents are established when silver nanoparticles (cathode) embedded in a titanium matrix (anode) are exposed to electrolytes^[45] - this galvanic coupling can cause changes in bacterial membrane morphology and DNA, leading to cell death^[37]. Silver-based coatings have antimicrobial efficacy against a broad spectrum of pathogens, including *Escherichia coli*, *S. aureus* and *S. epidermidis*^[46-48]. Using an *in vivo* model for osteomyelitis, Tran *et al.*^[48] inoculated *S. aureus* into fractured goat tibias and found after 5 wk silver-doped coated intramedullary nails led to better clinical and histology outcomes than the controls fixed with uncoated nails.

Early clinical studies have shown promising results with regard to reducing periprosthetic infections. Wafa *et al.*^[49] retrospectively compared 85 patients with silver-coated tumor prostheses to 85 tumor patients with non-silver tumor prostheses. The authors found that the average infection rate among silver-coated implant patients was 10.6% lower than that of their uncoated counterparts. In a similar prospective study by Harges *et al.*^[50], silver-coated prosthetic tumor implants were shown to have an 11.7% lower infection rate over a five-year period than uncoated implants. Despite these encouraging clinical results, clinical use of silver-coated implants has been limited by concerns of mammalian bone cell cytotoxicity^[51,52]. While this cytotoxic level is much lower than the anti-microbial threshold used for implant coatings, there is evidence to suggest that prolonged exposure to even low doses of nano-silver may result in mild toxicity in rats^[53]. The long-term implications of such toxicity are yet undetermined. Because of its long history of usage, and relatively low toxicity, silver-based antimicrobial coatings represent

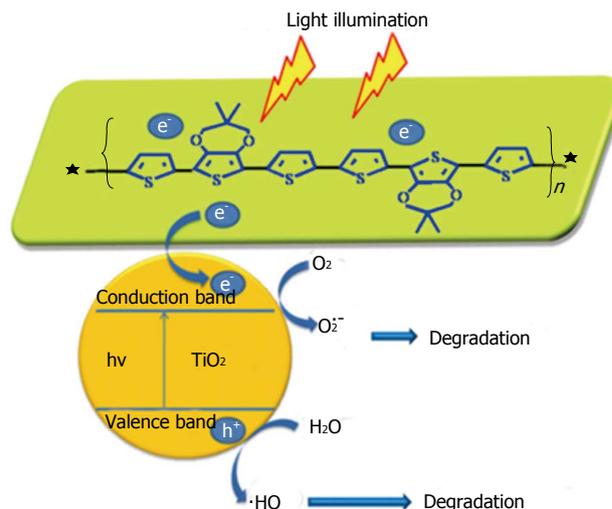


Figure 4 Schematic illustration of proposed photocatalytic and antibacterial mechanisms of a nanocomposite photocatalytic coating^[55]. TiO₂: Titanium oxide.

a very promising tool against antibiotic-resistant pathogens. The effectiveness of the technology has been shown to be largely dependent on the ability of the coating matrix to provide efficacious release kinetics and formulation of silver nanoparticles or ions.

Photoactive-based coatings

Photocatalyst coatings are composed of titanium alloys and display bactericidal effects *via* membrane degradation after activating exposure to ultraviolet irradiation (Figure 4)^[54,55]. Titanium oxide (TiO₂) is a commonly used photocatalytic agent due to its strong oxidizing power, lack of toxicity, and long-term chemical stability^[56]. Villatte *et al.*^[56] demonstrated TiO₂-based photoactive coatings were able to withstand mechanical stress from inserting stainless steel pins in cow femurs, had antibacterial effectiveness against *S. aureus* and *S. epidermidis* cultures, and has the added benefit of low cost and easy scalability. Photocatalysts as antimicrobial agents in orthopedic implants remain to be tested *in vivo*.

NON-COATING TECHNOLOGY

Antibiotic-loaded bone cement

In addition to coatings, several other antimicrobial orthopedic implant technologies are being evaluated. Antibiotic-loaded bone cement (ALBC), such as PMMA, is widely used by orthopedic surgeons to help secure arthroplasty implants, to fill bone voids, and to treat vertebral compression fractures (Figure 5)^[57,58]. ALBC has been in use since first being developed in 1970 as a potential method for *in situ* drug release^[59]. Despite its widespread use, the antimicrobial efficacy of ALBC is debated^[60,61]. Due to irregular release of antibiotic, only 5%-8% of the drug typically elutes properly^[62]. Therefore, the high doses needed for a therapeutic effect have been shown to produce pathogen resistance^[57].



Figure 5 Antibiotic loaded bone cement beads strung on braided stainless steel^[68].

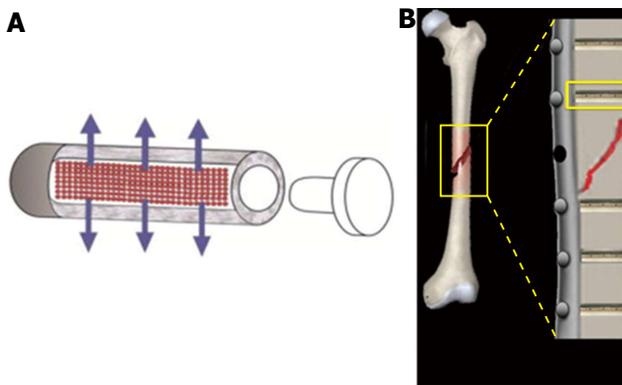


Figure 6 Fixation pins with tubular reservoirs for controlled drug release. Diagrams highlighting the principle design of fixation pins: A: Scheme of a drug releasing fixation pin. Note the permeation through the porous wall (arrows)^[64]; B: Scheme of implanted fixation pins, each capable of eluting local antibiotics around fixation site^[65].

Antibiotic-loaded reservoirs

A novel system utilizes antibiotic-loaded reservoirs within the steel implant itself to enable a more controlled, localized release of drug when compared to coatings^[63]. Initial *in vivo* testing by Gimeno *et al.*^[64] demonstrated that sheep infected with a biofilm-forming *S. aureus* strain showed no signs of infection of pre-placed tibia implants 7-9 d post introduction of *S. aureus*. Gimeno *et al.*^[65] subsequently proposed a design detailing fixation pins with tubular reservoirs for loading of antibiotics, allowing for more controlled release of the antibiotic based on number and size of release orifices (Figure 6).

Modified surface characteristics

Modifying implant surface characteristics have also been investigated as a means of reducing biofilm. For example, mixtures of polyethylene oxide and protein-repelling polyethylene glycol have shown significant bacterial inhibition when applied implant surfaces^[66,67]. Singh *et al.*^[68] demonstrated that modifying surface roughness (Figures 7^[69] and 8) of a material at the nanoscale level could provide antibacterial properties. Surface

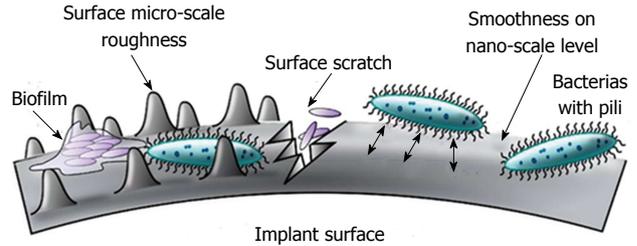


Figure 7 Interaction between surface roughness and bacterial adhesion^[69].

characteristic modification has been shown to interfere with osseointegration of the implants, challenging its clinical application^[70]. Other studies have shown that certain pathogens are able to adhere, proliferate, and form biofilms more readily on rough surfaces. The data available suggests there is threshold where modified surface microtopography can be an effective means of reducing biofilm, or encouraging bacterial growth.

Electrospinning

Electrospun matrices of PLGA nano-fibers have recently been proposed as a promising antimicrobial approach to orthopedic implant-associated infections^[71]. In electrospinning, ultrafine fibers with nanometer diameters form a matrix with a very high surface-area-to-volume ratio^[72]. Produced by syringe-pumping various drug and polymer solutions in the presence of a high electrical field potential^[73], the resulting drug loaded, non-woven PLGA membranes are flexible, porous, and enable controlled drug release (Figure 9)^[71,74]. Like coating, the matrices adhere directly to orthopedic implants.

Integrated biofilms

Özçelik *et al.*^[75] proposed a novel polyelectrolyte multilayer film approach using combined antimicrobial and immunomodulatory strategies (Figure 10). Composed of polyarginine and hyaluronic acid, the film inhibits the production of inflammatory cytokines, combats bacteria using a nanoscale silver coating, and opens the opportunity for bacteria-specific customization *via* embedded antimicrobial peptides. Although development of such films is far from clinical practice, microfilms are a promising look into the benefits of combining existing approaches for limiting implant-related complications to develop the composite technology of the future.

CONCLUSION

Several imperfect options exist for reducing the risk of orthopaedic implant infections. Despite technological advancement, orthopedic implant-associated infections remain as an important clinical problem, necessitating additional improvement. With promising technology on the horizon, it seems that the answer for reduced infection may not lie in solely one device or technology but in the synergy of many.

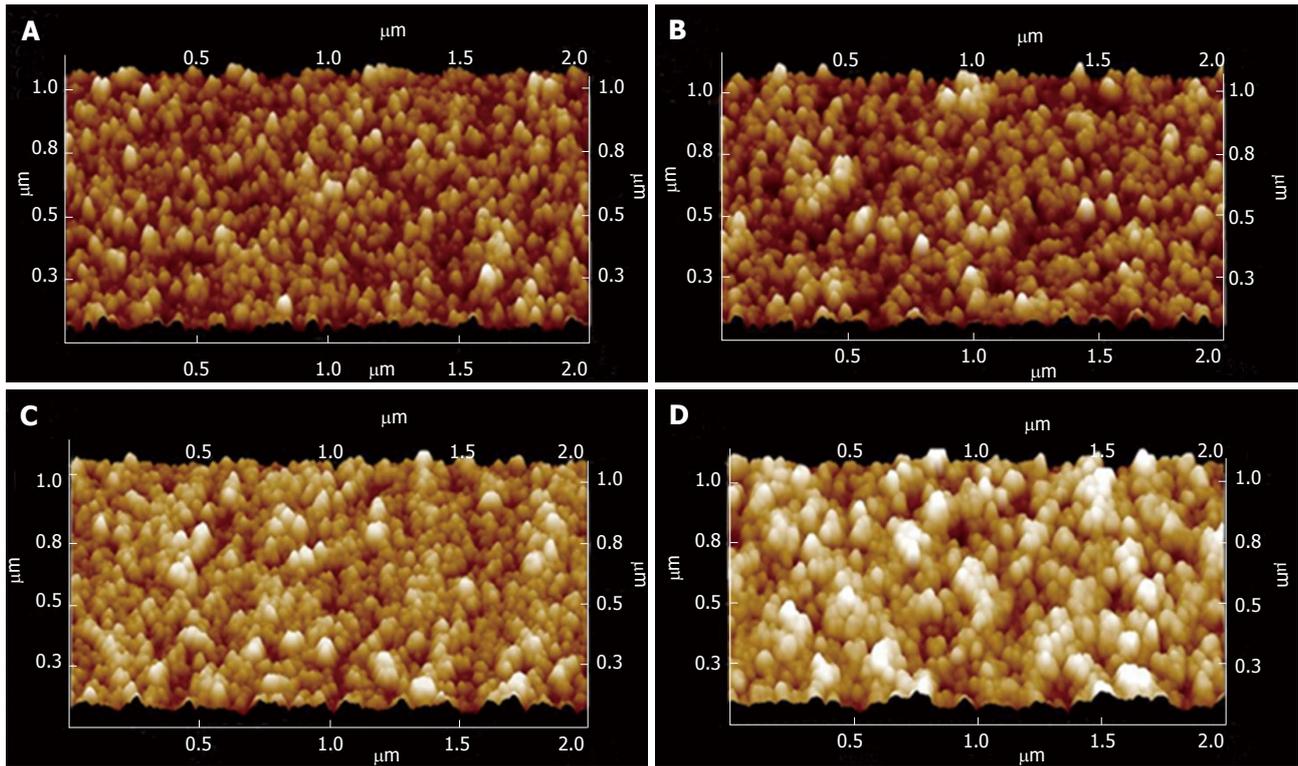


Figure 8 Atomic force microscopy of different surface film topography of increasing thickness (A: 50 nm; B: 100 nm; C: 200 nm; D: 300 nm)^[68].

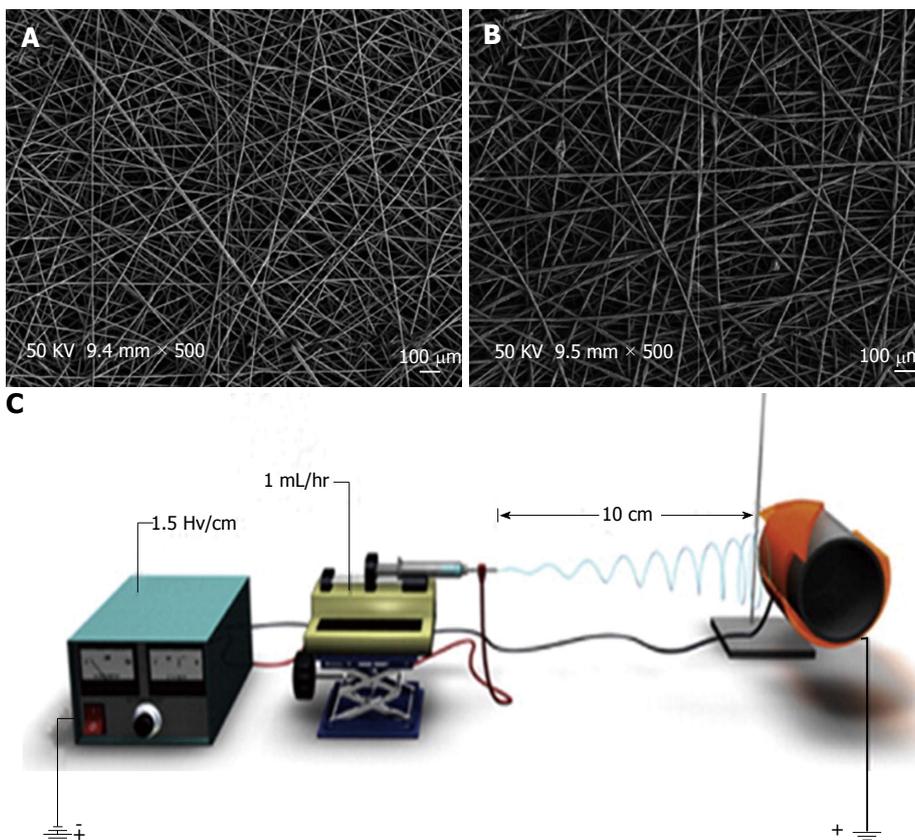


Figure 9 Micrograph and apparatus perspective of electrospinning technology. Scanning electron microscopy micrographs of PLGA electrospun coatings containing (A) vancomycin and (B) no drug^[74]; C: Schematic of a charged electrospinning apparatus spinning a PLGA coating onto an implant device^[71]. PLGA: Poly(lactic-co-glycolic acid).

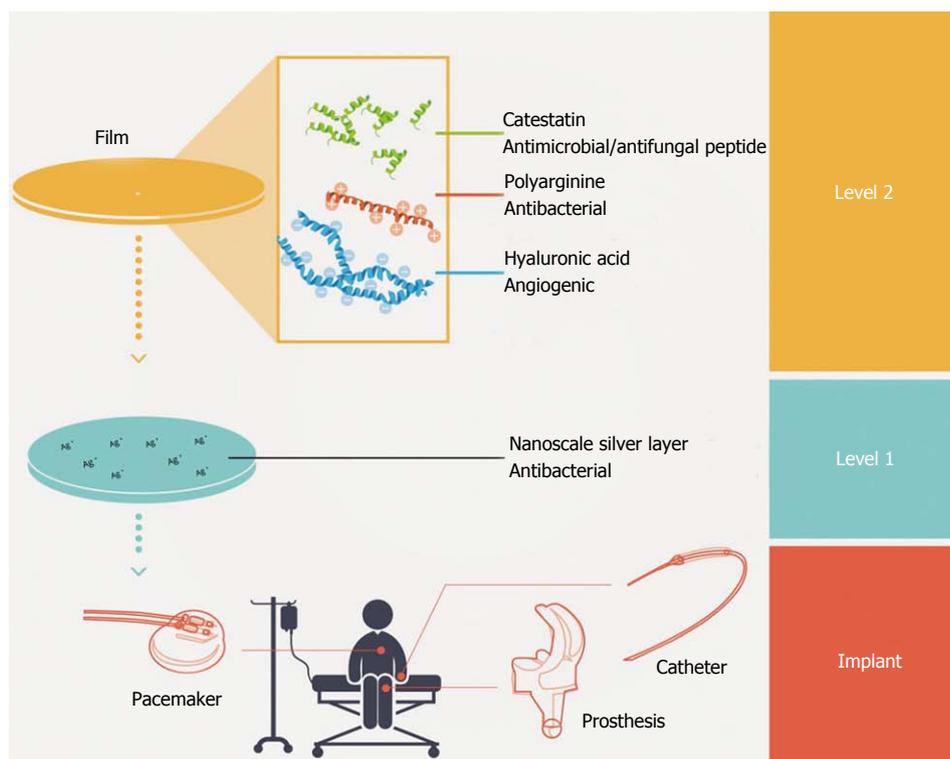


Figure 10 Integration of antimicrobial biofilms into the implant process^[75].

REFERENCES

- 1 Goodman SB, Yao Z, Keeney M, Yang F. The future of biologic coatings for orthopaedic implants. *Biomaterials* 2013; **34**: 3174-3183 [PMID: 23391496 DOI: 10.1016/j.biomaterials.2013.01.074]
- 2 Simon JP, Fabry G. An overview of implant materials. *Acta Orthop Belg* 1991; **57**: 1-5 [PMID: 2038938]
- 3 Moriarty TF, Schlegel U, Perren S, Richards RG. Infection in fracture fixation: can we influence infection rates through implant design? *J Mater Sci Mater Med* 2010; **21**: 1031-1035 [PMID: 19842017 DOI: 10.1007/s10856-009-3907-x]
- 4 Donlan RM. Biofilms: microbial life on surfaces. *Emerg Infect Dis* 2002; **8**: 881-890 [PMID: 12194761 DOI: 10.3201/eid0809.020063]
- 5 Stewart PS, Costerton JW. Antibiotic resistance of bacteria in biofilms. *Lancet* 2001; **358**: 135-138 [PMID: 11463434 DOI: 10.1016/S0140-6736(01)05321-1]
- 6 Jefferson KK, Goldmann DA, Pier GB. Use of confocal microscopy to analyze the rate of vancomycin penetration through *Staphylococcus aureus* biofilms. *Antimicrob Agents Chemother* 2005; **49**: 2467-2473 [PMID: 15917548 DOI: 10.1128/AAC.49.6.2467-2473.2005]
- 7 Luo J, Chen Z, Sun Y. Controlling biofilm formation with an N-halamine-based polymeric additive. *J Biomed Mater Res A* 2006; **77**: 823-831 [PMID: 16575910 DOI: 10.1002/jbm.a.30689]
- 8 Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med* 2004; **350**: 1422-1429 [PMID: 15070792 DOI: 10.1056/NEJMra035415]
- 9 Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999; **20**: 725-730 [PMID: 10580621 DOI: 10.1086/501572]
- 10 Bryan CS, Morgan SL, Caton RJ, Lunceford EM. Cefazolin versus cefamandole for prophylaxis during total joint arthroplasty. *Clin Orthop Relat Res* 1988; **(228)**: 117-122 [PMID: 3342553 DOI: 10.1097/00003086-198803000-00018]
- 11 Veerachamy S, Yarlagadda T, Manivasagam G, Yarlagadda PK. Bacterial adherence and biofilm formation on medical implants: a review. *Proc Inst Mech Eng H* 2014; **228**: 1083-1099 [PMID: 25406229 DOI: 10.1177/0954411914556137]
- 12 Wu P, Grainger DW. Drug/device combinations for local drug therapies and infection prophylaxis. *Biomaterials* 2006; **27**: 2450-2467 [PMID: 16337266 DOI: 10.1016/j.biomaterials.2005.11.031]
- 13 Avés EP, Estévez GF, Sader MS, Sierra JC, Yurell JC, Bastos IN, Soares GD. Hydroxyapatite coating by sol-gel on Ti-6Al-4V alloy as drug carrier. *J Mater Sci Mater Med* 2009; **20**: 543-547 [PMID: 19104913 DOI: 10.1007/s10856-008-3609-9]
- 14 Geesink RG, de Groot K, Klein CP. Bonding of bone to apatite-coated implants. *J Bone Joint Surg Br* 1988; **70**: 17-22 [PMID: 2828374]
- 15 Neut D, Dijkstra RJ, Thompson JI, van der Mei HC, Busscher HJ. A gentamicin-releasing coating for cementless hip prostheses-Longitudinal evaluation of efficacy using in vitro bio-optical imaging and its wide-spectrum antibacterial efficacy. *J Biomed Mater Res A* 2012; **100**: 3220-3226 [PMID: 22733713 DOI: 10.1002/jbm.a.34258]
- 16 Alt V, Bitschnau A, Osterling J, Sewing A, Meyer C, Kraus R, Meissner SA, Wenisch S, Domann E, Schnettler R. The effects of combined gentamicin-hydroxyapatite coating for cementless joint prostheses on the reduction of infection rates in a rabbit infection prophylaxis model. *Biomaterials* 2006; **27**: 4627-4634 [PMID: 16712926 DOI: 10.1016/j.biomaterials.2006.04.035]
- 17 Schmidmaier G, Lucke M, Wildemann B, Haas NP, Raschke M. Prophylaxis and treatment of implant-related infections by antibiotic-coated implants: a review. *Injury* 2006; **37** Suppl 2: S105-S112 [PMID: 16651063 DOI: 10.1016/j.injury.2006.04.016]
- 18 Fuchs T, Stange R, Schmidmaier G, Raschke MJ. The use of gentamicin-coated nails in the tibia: preliminary results of a prospective study. *Arch Orthop Trauma Surg* 2011; **131**: 1419-1425 [PMID: 21617934 DOI: 10.1007/s00402-011-1321-6]
- 19 Metsemakers WJ, Reul M, Nijs S. The use of gentamicin-coated nails in complex open tibia fracture and revision cases: A retrospective analysis of a single centre case series and review of

- the literature. *Injury* 2015; **46**: 2433-2437 [PMID: 26477343 DOI: 10.1016/j.injury.2015.09.028]
- 20 **ter Boo GJ**, Grijpma DW, Moriarty TF, Richards RG, Eglin D. Antimicrobial delivery systems for local infection prophylaxis in orthopedic- and trauma surgery. *Biomaterials* 2015; **52**: 113-125 [PMID: 25818418 DOI: 10.1016/j.biomaterials.2015.02.020]
 - 21 **Arciola CR**, Campoccia D, An YH, Baldassarri L, Pirini V, Donati ME, Pegreffì F, Montanaro L. Prevalence and antibiotic resistance of 15 minor staphylococcal species colonizing orthopedic implants. *Int J Artif Organs* 2006; **29**: 395-401 [PMID: 16705608]
 - 22 **Ambrose CG**, Clyburn TA, Mika J, Gogola GR, Kaplan HB, Wanger A, Mikos AG. Evaluation of antibiotic-impregnated microspheres for the prevention of implant-associated orthopaedic infections. *J Bone Joint Surg Am* 2014; **96**: 128-134 [PMID: 24430412 DOI: 10.2106/JBJS.L.01750]
 - 23 **Ambrose CG**, Gogola GR, Clyburn TA, Raymond AK, Peng AS, Mikos AG. Antibiotic microspheres: preliminary testing for potential treatment of osteomyelitis. *Clin Orthop Relat Res* 2003; **415**: 279-285 [PMID: 14612657 DOI: 10.1097/01.blo.0000093920.26658.ae]
 - 24 **Ambrose CG**, Clyburn TA, Loudon K, Joseph J, Wright J, Gulati P, Gogola GR, Mikos AG. Effective treatment of osteomyelitis with biodegradable microspheres in a rabbit model. *Clin Orthop Relat Res* 2004; **421**: 293-299 [PMID: 15123963 DOI: 10.1097/01.blo.0000126303.41711.a2]
 - 25 **Reading AD**, Rooney P, Taylor GJ. Quantitative assessment of the effect of 0.05% chlorhexidine on rat articular cartilage metabolism in vitro and in vivo. *J Orthop Res* 2000; **18**: 762-767 [PMID: 11117298 DOI: 10.1002/jor.1100180513]
 - 26 **Russell AD**, Day MJ. Antibacterial activity of chlorhexidine. *J Hosp Infect* 1993; **25**: 229-238 [PMID: 7907620 DOI: 10.1016/0195-6701(93)90109-D]
 - 27 **Cheung HY**, Wong MM, Cheung SH, Liang LY, Lam YW, Chiu SK. Differential actions of chlorhexidine on the cell wall of *Bacillus subtilis* and *Escherichia coli*. *PLoS One* 2012; **7**: e36659 [PMID: 22606280 DOI: 10.1371/journal.pone.0036659]
 - 28 **Kim HS**, Woo Chang S, Baek SH, Han SH, Lee Y, Zhu Q, Kum KY. Antimicrobial effect of alexidine and chlorhexidine against *Enterococcus faecalis* infection. *Int J Oral Sci* 2013; **5**: 26-31 [PMID: 23492900 DOI: 10.1038/ijos.2013]
 - 29 **DeJong ES**, DeBerardino TM, Brooks DE, Nelson BJ, Campbell AA, Bottoni CR, Pusateri AE, Walton RS, Guymon CH, McManus AT. Antimicrobial efficacy of external fixator pins coated with a lipid stabilized hydroxyapatite/chlorhexidine complex to prevent pin tract infection in a goat model. *J Trauma* 2001; **50**: 1008-1014 [PMID: 11426113 DOI: 10.1097/00005373-200106000-00006]
 - 30 **Ho KM**, Litton E. Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis. *J Antimicrob Chemother* 2006; **58**: 281-287 [PMID: 16757502 DOI: 10.1093/jac/dki234]
 - 31 **Yang CC**, Lin CC, Liao JW, Yen SK. Vancomycin-chitosan composite deposited on post porous hydroxyapatite coated Ti6Al4V implant for drug controlled release. *Mater Sci Eng C Mater Biol Appl* 2013; **33**: 2203-2212 [PMID: 23498249 DOI: 10.1016/j.msec.2013.01.038]
 - 32 **Magetsari PhD R**, Dewo PhD P, Saputro Md BK, Lanodiyu Md Z. Cinnamon Oil and Chitosan Coating on Orthopaedic Implant Surface for Prevention of *Staphylococcus Epidermidis* Biofilm Formation. *Malays Orthop J* 2014; **8**: 11-14 [PMID: 26401229 DOI: 10.5704/MOJ.1411.003]
 - 33 **Qin L**, Dong H, Mu Z, Zhang Y, Dong G. Preparation and bioactive properties of chitosan and casein phosphopeptides composite coatings for orthopedic implants. *Carbohydr Polym* 2015; **133**: 236-244 [PMID: 26344277 DOI: 10.1016/j.carbpol.2015.06.099]
 - 34 **Sondi I**, Salopek-Sondi B. Silver nanoparticles as antimicrobial agent: a case study on *E. coli* as a model for Gram-negative bacteria. *J Colloid Interface Sci* 2004; **275**: 177-182 [PMID: 15158396 DOI: 10.1016/j.jcis.2004.02.012]
 - 35 **Kim JS**, Kuk E, Yu KN, Kim JH, Park SJ, Lee HJ, Kim SH, Park YK, Park YH, Hwang CY, Kim YK, Lee YS, Jeong DH, Cho MH. Antimicrobial effects of silver nanoparticles. *Nanomedicine* 2007; **3**: 95-101 [PMID: 17379174]
 - 36 **Shrivastava S**, Bera T, Roy A, Singh G, Ramachandrarao P, Dash D. Characterization of enhanced antibacterial effects of novel silver nanoparticles. *Nanotechnology* 2007; **18**: 225103 [DOI: 10.1088/0957-4484/18/22/225103]
 - 37 **Morones JR**, Elechiguerra JL, Camacho A, Holt K, Kouri JB, Ramirez JT, Yacaman MJ. The bactericidal effect of silver nanoparticles. *Nanotechnology* 2005; **16**: 2346-2353 [PMID: 20818017 DOI: 10.1088/0957-4484/16/10/059]
 - 38 **Pal S**, Tak YK, Song JM. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the Gram-negative bacterium *Escherichia coli*. *Appl Environ Microbiol* 2007; **73**: 1712-1720 [PMID: 17261510]
 - 39 **Gosheger G**, Harges J, Ahrens H, Streitburger A, Buerger H, Erren M, Günsel A, Kemper FH, Winkelmann W, Von Eiff C. Silver-coated megaendoprostheses in a rabbit model--an analysis of the infection rate and toxicological side effects. *Biomaterials* 2004; **25**: 5547-5556 [PMID: 15142737]
 - 40 **Lee D**, Cohen RE, Rubner MF. Antibacterial properties of Ag nanoparticle loaded multilayers and formation of magnetically directed antibacterial microparticles. *Langmuir* 2005; **21**: 9651-9659 [PMID: 16207049]
 - 41 **Jung WK**, Koo HC, Kim KW, Shin S, Kim SH, Park YH. Antibacterial activity and mechanism of action of the silver ion in *Staphylococcus aureus* and *Escherichia coli*. *Appl Environ Microbiol* 2008; **74**: 2171-2178 [PMID: 18245232 DOI: 10.1128/AEM.02001-07]
 - 42 **Dal Lago V**, de Oliveira LF, de Almeida Gonçalves K, Kobargb J, Cardoso MB. Size-selective silver nanoparticles: future of biomedical devices with enhanced bactericidal properties. *J Mater Chem* 2011; **21**: 12267-12273 [DOI: 10.1039/C1JM12297E]
 - 43 **Knetsch ML**, Koole LH. New strategies in the development of antimicrobial coatings: the example of increasing usage of silver and silver nanoparticles. *Polymer* 2011; **3**: 340-366 [DOI: 10.3390/polym3010340]
 - 44 **Zheng Y**, Li J, Liu X, Sun J. Antimicrobial and osteogenic effect of Ag-implanted titanium with a nanostructured surface. *Int J Nanomedicine* 2012; **7**: 875-884 [PMID: 22393287 DOI: 10.2147/IJN.S28450]
 - 45 **Cao H**, Liu X, Meng F, Chu PK. Biological actions of silver nanoparticles embedded in titanium controlled by micro-galvanic effects. *Biomaterials* 2011; **32**: 693-705 [PMID: 20970183 DOI: 10.1016/j.biomaterials.2010.09.066]
 - 46 **Feng QL**, Wu J, Chen GQ, Cui FZ, Kim TN, Kim JO. A mechanistic study of the antibacterial effect of silver ions on *Escherichia coli* and *Staphylococcus aureus*. *J Biomed Mater Res* 2000; **52**: 662-668 [PMID: 11033548]
 - 47 **Tran N**, Kelley MN, Tran PA, Garcia DR, Jarrell JD, Hayda RA, Born CT. Silver doped titanium oxide-PDMS hybrid coating inhibits *Staphylococcus aureus* and *Staphylococcus epidermidis* growth on PEEK. *Mater Sci Eng C Mater Biol Appl* 2015; **49**: 201-209 [PMID: 25686940 DOI: 10.1016/j.msec.2014.12.072]
 - 48 **Tran N**, Tran PA, Jarrell JD, Engiles JB, Thomas NP, Young MD, Hayda RA, Born CT. In vivo caprine model for osteomyelitis and evaluation of biofilm-resistant intramedullary nails. *Biomed Res Int* 2013; **2013**: 674378 [PMID: 23841085 DOI: 10.1155/2013/674378]
 - 49 **Wafa H**, Grimer RJ, Reddy K, Jeys L, Abudu A, Carter SR, Tillman RM. Retrospective evaluation of the incidence of early periprosthetic infection with silver-treated endoprostheses in high-risk patients: case-control study. *Bone Joint J* 2015; **97-B**: 252-257 [PMID: 25628291 DOI: 10.1302/0301-620X.97B2.34554]
 - 50 **Harges J**, von Eiff C, Streitbuenger A, Balke M, Budny T, Henrichs MP, Hauschild G, Ahrens H. Reduction of periprosthetic infection with silver-coated megaprotheses in patients with bone sarcoma. *J Surg Oncol* 2010; **101**: 389-395 [PMID: 20119985 DOI: 10.1002/jso.21498]
 - 51 **Park MV**, Neigh AM, Vermeulen JP, de la Fonteyne LJ, Verharen HW, Briedé JJ, van Loveren H, de Jong WH. The effect of particle size on the cytotoxicity, inflammation, developmental toxicity

- and genotoxicity of silver nanoparticles. *Biomaterials* 2011; **32**: 9810-9817 [PMID: 21944826 DOI: 10.1016/j.biomaterials.2011.08.085]
- 52 **AshaRani PV**, Low Kah Mun G, Hande MP, Valiyaveetil S. Cytotoxicity and genotoxicity of silver nanoparticles in human cells. *ACS Nano* 2009; **3**: 279-290 [PMID: 19236062 DOI: 10.1021/nn800596w]
- 53 **Kim YS**, Kim JS, Cho HS, Rha DS, Kim JM, Park JD, Choi BS, Lim R, Chang HK, Chung YH, Kwon IH, Jeong J, Han BS, Yu IJ. Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. *Inhal Toxicol* 2008; **20**: 575-583 [PMID: 18444010 DOI: 10.1080/08958370701874663]
- 54 **Matsunaga T**, Tomoda R, Nakajima T, Wake H. Photoelectrochemical sterilization of microbial cells by semiconductor powders. *FEMS Microbiol Lett* 1985; **29**: 211-214 [DOI: 10.1111/j.1574-6968.1985.tb00864.x]
- 55 **Jamal R**, Osman Y, Rahman A, Ali A, Zhang Y, Abdiryim T. Solid-State Synthesis and Photocatalytic Activity of Polyterthiophene Derivatives/TiO₂ Nanocomposites. *Materials* 2014; **7**: 3786-3801 [DOI: 10.3390/ma7053786]
- 56 **Villatte G**, Massard C, Descamps S, Sibaud Y, Forestier C, Awitor KO. Photoactive TiO₂ antibacterial coating on surgical external fixation pins for clinical application. *Int J Nanomedicine* 2015; **10**: 3367-3375 [PMID: 26005347 DOI: 10.2147/IJN.S81518]
- 57 **Passuti N**, Gouin F. Antibiotic-loaded bone cement in orthopedic surgery. *Joint Bone Spine* 2003; **70**: 169-174 [PMID: 12814759 DOI: 10.1016/S1297-319X(03)00002-2]
- 58 **Samuel S**. Antibiotic Loaded Acrylic Bone Cement in Orthopaedic Trauma. In: Bapatista MS, editor. Osteomyelitis. InTech Publishers, Rijeka, Croatia
- 59 **Buchholz HW**, Engelbrecht H. [Depot effects of various antibiotics mixed with Palacos resins]. *Chirurg* 1970; **41**: 511-515 [PMID: 5487941]
- 60 **Yi Z**, Bin S, Jing Y, Zongke Z, Pengde K, Fuxing P. No decreased infection rate when using antibiotic-impregnated cement in primary total joint arthroplasty. *Orthopedics* 2014; **37**: 839-845 [PMID: 25437076 DOI: 10.3928/01477447-20141124-07]
- 61 **Kendall RW**, Duncan CP, Smith JA, Ngui-Yen JH. Persistence of bacteria on antibiotic loaded acrylic depots. A reason for caution. *Clin Orthop Relat Res* 1996; **329**: 273-280 [PMID: 8769462 DOI: 10.1097/00003086-199608000-00034]
- 62 **van de Belt H**, Neut D, Schenk W, van Horn JR, van der Mei HC, Busscher HJ. Gentamicin release from polymethylmethacrylate bone cements and Staphylococcus aureus biofilm formation. *Acta Orthop Scand* 2000; **71**: 625-629 [PMID: 11145392]
- 63 **Perez LM**, Lalueza P, Monzon M, Puertolas JA, Arruebo M, Santamaria J. Hollow porous implants filled with mesoporous silica particles as a two-stage antibiotic-eluting device. *Int J Pharm* 2011; **409**: 1-8 [PMID: 21335077 DOI: 10.1016/j.ijpharm.2011.02.015]
- 64 **Gimeno M**, Pinczowski P, Vázquez FJ, Pérez M, Santamaria J, Arruebo M, Luján L. Porous orthopedic steel implant as an antibiotic eluting device: prevention of post-surgical infection on an ovine model. *Int J Pharm* 2013; **452**: 166-172 [PMID: 23651643 DOI: 10.1016/j.ijpharm.2013.04.076]
- 65 **Gimeno M**, Pinczowski P, Pérez M, Giorello A, Martínez MÁ, Santamaria J, Arruebo M, Luján L. A controlled antibiotic release system to prevent orthopedic-implant associated infections: An in vitro study. *Eur J Pharm Biopharm* 2015; **96**: 264-271 [PMID: 26297104 DOI: 10.1016/j.ejpb.2015.08.007]
- 66 **Kaper HJ**, Busscher HJ, Norde W. Characterization of poly (ethylene oxide) brushes on glass surfaces and adhesion of Staphylococcus epidermidis. *J Biomater Sci Polym Ed* 2003; **14**: 313-324 [PMID: 12747672]
- 67 **Zhang F**, Zhang Z, Zhu X, Kang ET, Neoh KG. Silk-functionalized titanium surfaces for enhancing osteoblast functions and reducing bacterial adhesion. *Biomaterials* 2008; **29**: 4751-4759 [PMID: 18829101 DOI: 10.1016/j.biomaterials.2008.08.043]
- 68 **Singh AV**, Vyas V, Patil R, Sharma V, Scopelliti PE, Bongiorno G, Podestà A, Lenardi C, Gade WN, Milani P. Quantitative characterization of the influence of the nanoscale morphology of nanostructured surfaces on bacterial adhesion and biofilm formation. *PLoS One* 2011; **6**: e25029 [PMID: 21966403 DOI: 10.1371/journal.pone.0025029]
- 69 **Gallo J**, Holinka M, Moucha CS. Antibacterial surface treatment for orthopaedic implants. *Int J Mol Sci* 2014; **15**: 13849-13880 [PMID: 25116685 DOI: 10.3390/ijms150813849]
- 70 **Braem A**, Van Mellaert L, Mattheys T, Hofmans D, De Waelheyns E, Geris L, Anné J, Schrooten J, Vleugels J. Staphylococcal biofilm growth on smooth and porous titanium coatings for biomedical applications. *J Biomed Mater Res A* 2014; **102**: 215-224 [PMID: 23661274 DOI: 10.1002/jbm.a.34688]
- 71 **Gilchrist SE**, Lange D, Letchford K, Bach H, Fazli L, Burt HM. Fusidic acid and rifampicin co-loaded PLGA nanofibers for the prevention of orthopedic implant associated infections. *J Control Release* 2013; **170**: 64-73 [PMID: 23639451 DOI: 10.1016/j.jconrel.2013.04.012]
- 72 **Reneker DH**, Chun I. Nanometer diameter fibers of polymer, produced by electrospinning. *Nanotechnology* 1996; **7**: 216-223 [DOI: 10.1088/0957-4484/7/3/009]
- 73 **Reneker DH**, Yarin AL, Fong H, Koombhongse S. Bending instability of electrically charged liquid jets of polymer solutions in electrospinning. *J Appl Phys* 2000; **87**: 4531-4547 [DOI: 10.1063/1.373532]
- 74 **Zhang L**, Yan J, Yin Z, Tang C, Guo Y, Li D, Wei B, Xu Y, Gu Q, Wang L. Electrospun vancomycin-loaded coating on titanium implants for the prevention of implant-associated infections. *Int J Nanomedicine* 2014; **9**: 3027-3036 [PMID: 25028544 DOI: 10.2147/IJN.S63991]
- 75 **Özçelik H**, Vrana NE, Gudima A, Riabov V, Gratchev A, Haikel Y, Metz-Boutigue MH, Carradó A, Faerber J, Roland T, Klüter H, Kzhyshkowska J, Schaff P, Lavalle P. Harnessing the multifunctionality in nature: a bioactive agent release system with self-antimicrobial and immunomodulatory properties. *Adv Health Mater* 2015; **4**: 2026-2036 [PMID: 26379222 DOI: 10.1002/adhm.201500546]

P- Reviewer: Kelesidis T, Rouabhia M

S- Editor: Ji FF L- Editor: A E- Editor: Li D



Orthopedic disorders of the knee in hemophilia: A current concept review

E Carlos Rodriguez-Merchan, Leonard A Valentino

E Carlos Rodriguez-Merchan, Department of Orthopedic Surgery, La Paz University Hospital-IdiPaz, 28046 Madrid, Spain

Leonard A Valentino, Rush University Medical Center, Chicago, IL 60612, United States

Author contributions: Rodriguez-Merchan EC and Valentino LA wrote the article and reviewed the literature.

Conflict-of-interest statement: The authors declare no conflicts of interest for this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: E Carlos Rodriguez-Merchan, MD, PhD, Department of Orthopedic Surgery, La Paz University Hospital-IdiPaz, Paseo de la Castellana 261, 28046 Madrid, Spain. ecrmerchan@gmx.es
Telephone: +34-91-5712871
Fax: +34-91-5712871

Received: January 8, 2016

Peer-review started: January 12, 2016

First decision: March 1, 2016

Revised: April 7, 2016

Accepted: April 21, 2016

Article in press: April 22, 2016

Published online: June 18, 2016

Abstract

The knee is frequently affected by severe orthopedic changes known as hemophilic arthropathy (HA) in patients with deficiency of coagulation factor VIII or IX

and thus this manuscript seeks to present a current perspective of the role of the orthopedic surgeon in the management of these problems. Lifelong factor replacement therapy (FRT) is optimal to prevent HA, however adherence to this regerous treatment is challenging leading to breakthrough bleeding. In patients with chronic hemophilic synovitis, the prelude to HA, radiosynovectomy (RS) is the optimal to ameliorate bleeding. Surgery in people with hemophilia (PWH) is associated with a high risk of bleeding and infection, and must be performed with FRT. A coordinated effort including orthopedic surgeons, hematologists, physical medicine and rehabilitation physicians, physiotherapists and other team members is key to optimal outcomes. Ideally, orthopedic procedures should be performed in specialized hospitals with experienced teams. Until we are able to prevent orthopedic problems of the knee in PWH will have to continue performing orthopedic procedures (arthrocentesis, RS, arthroscopic synovectomy, hamstring release, arthroscopic debridement, alignment osteotomy, and total knee arthroplasty). By using the aforementioned procedures, the quality of life of PWH will be improved.

Key words: Hemophilia; Knee; Orthopedic problems; Prevention; Surgical treatment

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Hemophilia is an inherited bleeding disorder due to deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B) resulting in insufficient thrombin generation leading to recurrent intra-articular hemorrhages (hemarthroses). Prevention of hemarthroses with intravenous infusions of the deficient protein from infancy to adulthood (primary prophylaxis) should be considered to achieve optimal outcomes. If factor replacement therapy (FRT) is insufficient, or if patients are not adherent to the prescribed regimen, recurrent hemarthroses results in chondrocyte apoptosis (cartilage

degeneration) and hypertrophy of the synovium (synovitis). Many surgical interventions are available for the knee joint. For example, to treat synovitis recalcitrant to FRT, there are two primary orthopedic modalities: Radiosynovectomy and arthroscopic synovectomy. This article reviews the pathogenesis, diagnosis and treatment of hemophilic arthropathy of the knee.

Rodriguez-Merchan EC, Valentino LA. Orthopedic disorders of the knee in hemophilia: A current concept review. *World J Orthop* 2016; 7(6): 370-375 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/370.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.370>

INTRODUCTION

Hemophilic arthropathy (HA) in one or more joints, mainly ankles, elbows and knees affects about 90% of people with hemophilia (PWH) by 20-30 years of age (Figure 1). Recurrent bleeding into joints (hemarthroses) results in progressive, proliferative and degenerative articular changes. To prevent these complications, regular factor replacement therapy (FRT) with the deficient protein from an early age (primary prophylaxis) is the key to prevent synovitis and HA. However, despite primary prophylaxis, some PWH suffer from clinical bleeding due to an insufficient dosing regimen or non-adherence while others may experience subclinical joint bleeding. Although the pathogenesis of HA is not fully understood^[1], it is generally assumed that primary prophylaxis prevents bleeding and HA^[2,3].

There are multiple strategies for implementing primary prophylaxis in young children with severe hemophilia including once-weekly injections which has the advantage of avoiding the implantation of a central venous access device in very young children. Unfortunately, this regimen fails to prevent joint bleeding in all but a few children and most develop HA^[4].

Prophylaxis must begin early in life because even infrequent or a short durations of blood in contact with cartilage can cause chondrocyte apoptosis that can eventually lead to HA. Once developed, HA can be addressed with basic surgical procedures including radiosynovectomy (RS), chemical synovectomy (CS), arthroscopic synovectomy (AS), arthroscopic joint debridement and total knee arthroplasty (TKA)^[5,6].

RESEARCH

A literature review of knee disorders in patients with hemophilia was performed using MEDLINE (PubMed) and the Cochrane Library. The keywords used were "knee" and "hemophilia". The time period of the searches was from the beginning of the availability of the search engines until 31 December 2015. A total of 767 articles were found, of which 56 were selected and reviewed because they were deeply focused on the topic. The flow

diagram of the study is shown in Figure 2.

PATHOGENESIS

Chronic hemophilic synovitis (CHS) and cartilage destruction are the main findings of HA, both phenomena due to severe or recurrent hemarthroses. The precise pathogenesis of CHS and HA remains poorly understood. *Ex vivo* studies with canine cartilage suggest that a 4-d duration of blood exposure produces loss of cartilage matrix^[7]. Experimental studies have also demonstrated that after a major hemarthrosis the joint cavity is filled with a dense inflammatory infiltrate, and the tissues become brown-stained due to hemosiderin deposition following the breakdown of erythrocytes^[8,9]. Vascular hyperplasia takes place resulting in tenuous and friable vessels prone to bleed creating a viscous cycle of bleeding-vascular hyperplasia-bleeding. The articular surface becomes rugose with pannus formation and the subchondral bone becomes dysmorphic. After about one month, cartilage and bone erosions are evident.

It has been reported that the loading of the affected joint may play a role in the mechanism of cartilage degeneration in hemophilia^[10]. Other authors have found that molecular changes induced by iron in the blood could explain the increase in cell proliferation in the synovial membrane (synovitis)^[11]. Valentino *et al*^[12] found in an experimental murine model that hemorrhage induced by a controlled, blunt trauma injury leads to causes joint inflammation, synovitis and HA.

DIAGNOSIS

The diagnosis of CHS is usually made following examination of the knee with typical signs of joint swelling and warmth but with or without painful symptoms and reductions in motion of the knee. Ultrasonography (US) can be used to demonstrate hypertrophy of the synovium and the presence of fluid^[13,14]. However, validation of US for the assessment of HA has not been established yet^[15-17]. Magnetic resonance imaging is the gold standard for the diagnosis of synovitis.

ORTHOPEDIC TREATMENT

CHS

Celecoxib: Rattray *et al*^[18] reported that celecoxib is effective in treating hemophilic synovitis, although the mechanism for this effect remains to be determined and these findings require controlled trials to be confirmed.

RS: RS is the optimal choice for treatment of patients with CHS, even in patients with anti-factor antibodies (inhibitors)^[19-23]. The current recommendation is to use Yttrium-90 for the knees and Rhenium-186 for elbows and ankles and is supported by more than 40-years of experience with RS by the authors, who believe that the procedure is safe, easy to perform and economical technique for the management of CHS.

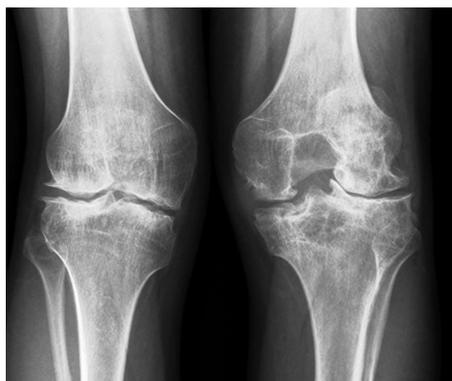


Figure 1 Severe bilateral hemophilic arthropathy of the knee in a 37-year-old male.

CS: Many chemical agents have been proposed to scar the synovium of patients with CHS including oral D-penicillamine^[24]. A short-term period (3-6 mo) of treatment at a dose of 5-10 mg/kg per day for children and less than 750 mg/d for adults (one hour before breakfast) was recommended. The efficacy of this treatment needs further clinical trial data before it will gain widespread use. Oral D-penicillamine may be especially useful in patients with inhibitors. Another method to perform CS is by means of intra-articular injections of rifampicin^[25] or oxytetracycline^[26]. Alternative, RS is a favorable alternative to oral D-penicillamine and to rifampicin or oxytetracycline for synovectomy, because its efficacy has been proven over the last 40 years^[27].

AS: The goal of AS is to reduce the number of hemarthroses in order to maintain the range of motion of the knee joint. However, AS cannot prevent joint degeneration^[28-32].

Advanced HA

Open and arthroscopic debridement: Both open and arthroscopic debridement with synovectomy has been used in PWH between 20 and 40 years of age, with improvement in pain lasting several years, delaying the need of a TKA^[33-35].

Hamstring release: Fixed knee flexion contracture is a common complication in PWH and hamstring tenotomy in association with posterior capsulotomy may be used to improve ambulation by reducing the contraction^[36,37].

External fixation for flexion contracture: More drastic measures have also been used to reduce flexion contractures. For example, Kiely *et al.*^[38] reported the case of a 13-year-old boy with hemophilia who underwent Ilizarov external fixator with improvement of his knee flexion contracture. In this case, progressive extension reduced the contracture from 50 to 5 degrees.

Osteotomies around the knee: Malalignment of the lower limb is common in hemophilia patients and

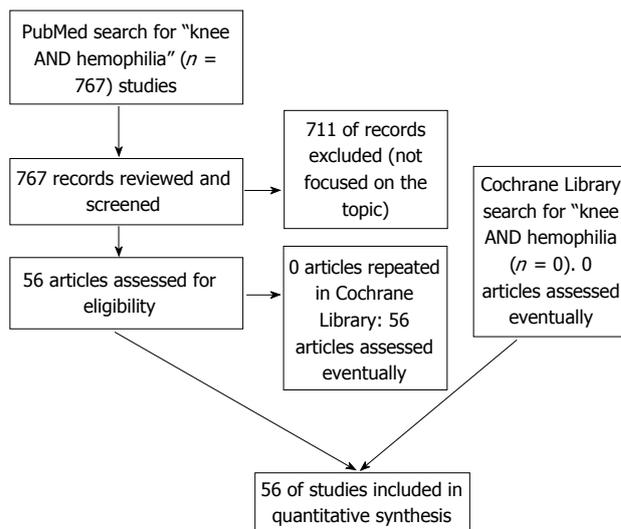


Figure 2 Flow chart of our search strategy.

osteotomy around the knee (proximal tibia, distal femur) has resulted in improvements in gait and reduction in painful symptoms^[39-42].

TKA: Unfortunately, many patients with knee HA continue to deteriorate resulting in life-altering knee pain. For these individuals, TKA is the treatment of choice and has resulted in dramatic improvements in patients with severe HA^[43-49]. Therefore, TKA is an excellent option for the treatment of advanced HA of the knee (Figure 3). However the procedure is not without risk as the rate of infection after TKA is 7% on average.

HEMATOLOGICAL PERIOPERATIVE TREATMENT

In major orthopedic procedures the preoperative levels of the deficient factor should be maintained at 80%-100%. In the postoperative period factor level must be over 50% in the two weeks and 30% later on, at least until wound healing (removal of staples)^[50,51]. Continuous infusion of the deficient factor is better than bolus infusion^[52,53] however mechanical malfunction of the venous line and pump must be guarded against. In patients with inhibitors there are two potential hematological treatments: Recombinant factor VII activated or Factor Eight Inhibitor Bypassing Agent^[54-57].

CONCLUSION

The best treatment for PWH is primary prophylaxis replacing the deficient clotting factor with early institution of regular injections of concentrates of factor VIII or IX. In this way, not only is bleeding into the joints prevented but also the development of synovitis and articular degeneration (HA). For CHS recalcitrant to aggressive factor replacement, RS must be considered the first option and alternatively, AS. Surgery in PWH has a high

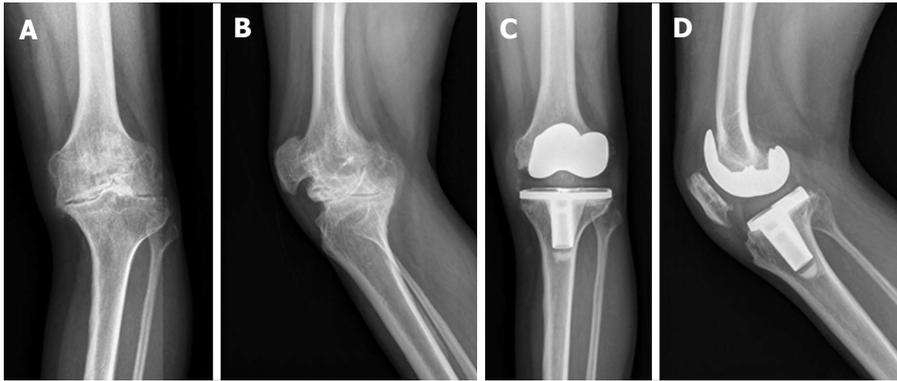


Figure 3 Severe painful hemophilic arthropathy of the left knee in a 41-year-old male. A cemented total knee arthroplasty (NexGen, Zimmer, United States) was performed with a satisfactory result: A: Anteroposterior preoperative radiograph; B: Lateral preoperative view; C: Anteroposterior radiograph 5 years later; D: Lateral view at 5 years. The quality of life of this patient improved significantly.

risk of bleeding and infection. This kind of surgery must be performed with FRT in a specialized center. This way we will improve the quality of life of PWH minimizing the risk of complications.

REFERENCES

- 1 **Lafeber FP**, Miossec P, Valentino LA. Physiopathology of haemophilic arthropathy. *Haemophilia* 2008; **14** Suppl 4: 3-9 [PMID: 18494686 DOI: 10.1111/j.1365-2516.2008.01732.x]
- 2 **Nilsson IM**, Berntorp E, Löfqvist T, Pettersson H. Twenty-five years' experience of prophylactic treatment in severe haemophilia A and B. *J Intern Med* 1992; **232**: 25-32 [PMID: 1640190 DOI: 10.1111/j.1365-2796.1992.tb00546.x]
- 3 **Manco-Johnson MJ**, Abshire TC, Shapiro AD, Riske B, Hacker MR, Kilcoyne R, Ingram JD, Manco-Johnson ML, Funk S, Jacobson L, Valentino LA, Hoots WK, Buchanan GR, DiMichele D, Recht M, Brown D, Leissing C, Bleak S, Cohen A, Mathew P, Matsunaga A, Medeiros D, Nugent D, Thomas GA, Thompson AA, McRedmond K, Soucie JM, Austin H, Evatt BL. Prophylaxis versus episodic treatment to prevent joint disease in boys with severe hemophilia. *N Engl J Med* 2007; **357**: 535-544 [PMID: 17687129 DOI: 10.1056/NEJMoa067659]
- 4 **Kraft J**, Blanchette V, Babyn P, Feldman B, Cloutier S, Israels S, Pai M, Rivard GE, Gomer S, McLimont M, Moineddin R, Doria AS. Magnetic resonance imaging and joint outcomes in boys with severe hemophilia A treated with tailored primary prophylaxis in Canada. *J Thromb Haemost* 2012; **10**: 2494-2502 [PMID: 23067060 DOI: 10.1111/jth.12025]
- 5 **Hilgartner MW**. Current treatment of hemophilic arthropathy. *Curr Opin Pediatr* 2002; **14**: 46-49 [PMID: 11880733 DOI: 10.1097/00008480-200202000-00008]
- 6 **Rodriguez-Merchan EC**. Aspects of current management: orthopaedic surgery in haemophilia. *Haemophilia* 2012; **18**: 8-16 [PMID: 21535324 DOI: 10.1111/j.1365-2516.2011.02544.x]
- 7 **Jansen NW**, Roosendaal G, Bijlsma JW, Degroot J, Lafeber FP. Exposure of human cartilage tissue to low concentrations of blood for a short period of time leads to prolonged cartilage damage: an in vitro study. *Arthritis Rheum* 2007; **56**: 199-207 [PMID: 17195222 DOI: 10.1002/art.22304]
- 8 **Valentino LA**, Hakobyan N. Histological changes in murine haemophilic synovitis: a quantitative grading system to assess blood-induced synovitis. *Haemophilia* 2006; **12**: 654-662 [PMID: 17083517 DOI: 10.1111/j.1365-2516.2006.01348.x]
- 9 **Valentino LA**, Hakobyan N, Rodriguez N, Hoots WK. Pathogenesis of haemophilic synovitis: experimental studies on blood-induced joint damage. *Haemophilia* 2007; **13** Suppl 3: 10-13 [PMID: 17822515 DOI: 10.1111/j.1365-2516.2007.01534.x]
- 10 **Hooiveld MJ**, Roosendaal G, Jacobs KM, Vianen ME, van den Berg HM, Bijlsma JW, Lafeber FP. Initiation of degenerative joint damage by experimental bleeding combined with loading of the joint: a possible mechanism of hemophilic arthropathy. *Arthritis Rheum* 2004; **50**: 2024-2031 [PMID: 15188380 DOI: 10.1002/art.20284]
- 11 **Hakobyan N**, Kazarian T, Jabbar AA, Jabbar KJ, Valentino LA. Pathobiology of hemophilic synovitis I: overexpression of mdm2 oncogene. *Blood* 2004; **104**: 2060-2064 [PMID: 15172967 DOI: 10.1182/blood-2003-12-4231]
- 12 **Valentino LA**, Hakobyan N, Kazarian T, Jabbar KJ, Jabbar AA. Experimental haemophilic synovitis: rationale and development of a murine model of human factor VIII deficiency. *Haemophilia* 2004; **10**: 280-287 [PMID: 15086328 DOI: 10.1111/j.1365-2516.2004.00899.x]
- 13 **Acharya SS**, Schloss R, Dyke JP, Mintz DN, Christos P, DiMichele DM, Adler RS. Power Doppler sonography in the diagnosis of hemophilic synovitis--a promising tool. *J Thromb Haemost* 2008; **6**: 2055-2061 [PMID: 18823337 DOI: 10.1111/j.1538-7836.2008.03160.x]
- 14 **Querol F**, Rodriguez-Merchan EC. The role of ultrasonography in the diagnosis of the musculo-skeletal problems of haemophilia. *Haemophilia* 2012; **18**: e215-e226 [PMID: 22044728 DOI: 10.1111/j.1365-2516.2011.02680.x]
- 15 **Merchan EC**, De Orbe A, Gago J. Ultrasound in the diagnosis of the early stages of hemophilic arthropathy of the knee. *Acta Orthop Belg* 1992; **58**: 122-125 [PMID: 1632211]
- 16 **Wallny T**, Brackmann HH, Semper H, Schumpe G, Effenberger W, Hess L, Seuser A. Intra-articular hyaluronic acid in the treatment of hemophilic arthropathy of the knee. Clinical, radiological and sonographical assessment. *Haemophilia* 2000; **6**: 566-570 [PMID: 11012703 DOI: 10.1046/j.1365-2516.2000.00413.x]
- 17 **Klukowska A**, Czyrny Z, Laguna P, Brzewski M, Serafin-Krol MA, Rokicka-Milewska R. Correlation between clinical, radiological and ultrasonographical image of knee joints in children with haemophilia. *Haemophilia* 2001; **7**: 286-292 [PMID: 11380633 DOI: 10.1046/j.1365-2516.2001.00509.x]
- 18 **Rattray B**, Nugent DJ, Young G. Celecoxib in the treatment of haemophilic synovitis, target joints, and pain in adults and children with haemophilia. *Haemophilia* 2006; **12**: 514-517 [PMID: 16919082 DOI: 10.1111/j.1365-2516.2006.01311.x]
- 19 **Rodriguez-Merchan EC**, Wiedel JD. General principles and indications of synoviorthesis (medical synovectomy) in haemophilia. *Haemophilia* 2001; **7** Suppl 2: 6-10 [PMID: 11564137 DOI: 10.1046/j.1365-2516.2001.00102.x]
- 20 **Rodriguez-Merchan EC**, Luck JV Jr, Silva M, Quintana M. Synoviorthesis in haemophilia. In: *The Haemophilic Joints-New Perspectives*. Rodriguez-Merchan EC, editor. Blackwell, Oxford, 2003: 73-79 [DOI: 10.1002/9780470986929.ch12]
- 21 **Mortazavi SM**, Asadollahi S, Farzan M, Shahriaran S, Aghili M, Izadyar S, Lak M. (32)P colloid radiosynovectomy in treat-

- ment of chronic haemophilic synovitis: Iran experience. *Haemophilia* 2007; **13**: 182-188 [PMID: 17286772 DOI: 10.1111/j.1365-2516.2006.01424.x]
- 22 **De la Corte-Rodriguez H**, Rodriguez-Merchan EC, Jimenez-Yuste V. Radiosynovectomy in hemophilia: quantification of its effectiveness through the assessment of 10 articular parameters. *J Thromb Haemost* 2011; **9**: 928-935 [PMID: 21352468 DOI: 10.1111/j.1538-7836.2011.04246.x]
- 23 **de la Corte-Rodriguez H**, Rodriguez-Merchan EC, Jimenez-Yuste V. What patient, joint and isotope characteristics influence the response to radiosynovectomy in patients with haemophilia? *Haemophilia* 2011; **17**: e990-e998 [PMID: 21535325 DOI: 10.1111/j.1365-2516.2011.02546.x]
- 24 **Corrigan JJ**, Damiano ML, Leissinger C, Wulff K. Treatment of chronic haemophilic synovitis in humans with D-penicillamine. *Haemophilia* 2003; **9**: 64-68 [PMID: 12558781 DOI: 10.1046/j.1365-2516.2003.00676.x]
- 25 **Radossi P**, Baggio R, Petris U, De Biasi E, Risato R, Davoli PG, Tagariello G. Intra-articular rifamycin in haemophilic arthropathy. *Haemophilia* 2003; **9**: 60-63 [PMID: 12558780 DOI: 10.1046/j.1365-2516.2003.00703.x]
- 26 **Fernandez-Palazzi F**, Viso R, Bernal R, Capetillo G, Caviglia H. Oxytetracycline clorhydrate as a new material for chemical synoviorthesis in haemophilia. In: *The Haemophilic Joints-New Perspectives*. Rodriguez-Merchan EC, editor. Blackwell, Oxford, 2003: 80-83 [DOI: 10.1002/9780470986929.ch13]
- 27 **Rodriguez-Merchán EC**. Orthopedic surgery is possible in hemophilic patients with inhibitors. *Am J Orthop (Belle Mead NJ)* 2012; **41**: 570-574 [PMID: 23431528]
- 28 **Wiedel JD**. Arthroscopic synovectomy for chronic hemophilic synovitis of the knee. *Arthroscopy* 1985; **1**: 205-209 [PMID: 4096772 DOI: 10.1016/S0749-8063(85)80013-X]
- 29 **Wiedel JD**. Arthroscopic synovectomy of the knee in hemophilia: 10-to-15 year followup. *Clin Orthop Relat Res* 1996; **328**: 46-53 [PMID: 8653977 DOI: 10.1097/00003086-199607000-00010]
- 30 **Journeycake JM**, Miller KL, Anderson AM, Buchanan GR, Finnegan M. Arthroscopic synovectomy in children and adolescents with hemophilia. *J Pediatr Hematol Oncol* 2003; **25**: 726-731 [PMID: 12972809 DOI: 10.1097/00043426-200309000-00010]
- 31 **Dunn AL**, Busch MT, Wyly JB, Sullivan KM, Abshire TC. Arthroscopic synovectomy for hemophilic joint disease in a pediatric population. *J Pediatr Orthop* 2004; **24**: 414-426 [PMID: 15205625 DOI: 10.1097/01241398-200407000-00013]
- 32 **Yoon KH**, Bae DK, Kim HS, Song SJ. Arthroscopic synovectomy in haemophilic arthropathy of the knee. *Int Orthop* 2005; **29**: 296-300 [PMID: 16082543 DOI: 10.1007/s00264-005-0666-2]
- 33 **Soreff J**. Joint debridement in the treatment of advanced hemophilic knee arthropathy. *Clin Orthop Relat Res* 1984; **191**: 179-184 [PMID: 6499309 DOI: 10.1097/00003086-198412000-00023]
- 34 **Rodriguez-Merchan EC**, Gomez-Cardero P. Arthroscopic knee debridement can delay total knee replacement in painful moderate haemophilic arthropathy of the knee in adult patients. *Blood Coagul Fibrinolysis* 2015; Epub ahead of print [PMID: 26575489 DOI: 10.1097/MBC.0000000000000443]
- 35 **Rodriguez Merchan EC**, Magallon M, Galindo E. Joint debridement for haemophilic arthropathy of the knee. *Int Orthop* 1994; **18**: 135-138 [PMID: 7927961]
- 36 **Rodriguez-Merchán EC**, Magallón M, Galindo E, López-Cabarcos C. Hamstring release for fixed knee flexion contracture in hemophilia. *Clin Orthop Relat Res* 1997; **34**: 63-67 [PMID: 9345208]
- 37 **Pennekamp PH**, Wallny TA, Goldmann G, Kraft CN, Berdel P, Oldenburg J, Wirtz DC. [Flexion contracture in haemophilic knee arthropathy--10-year follow-up after hamstring release and dorsal capsulotomy]. *Z Orthop Unfall* 2007; **145**: 317-321 [PMID: 17607630]
- 38 **Kiely PD**, McMahon C, Smith OP, Moore DP. The treatment of flexion contracture of the knee using the Ilizarov technique in a child with haemophilia B. *Haemophilia* 2003; **9**: 336-339 [PMID: 12694527 DOI: 10.1046/j.1365-2516.2003.00753.x]
- 39 **Rodriguez Merchan EC**, Galindo E. Proximal tibial valgus osteotomy for hemophilic arthropathy of the knee. *Orthop Rev* 1992; **21**: 204-208 [PMID: 1538887]
- 40 **Caviglia HA**, Perez-Bianco R, Galatro G, Duhalde C, Tezanos-Pinto M. Extensor supracondylar femoral osteotomy as treatment for flexed haemophilic knee. *Haemophilia* 1999; **5** Suppl 1: 28-32 [PMID: 10365298 DOI: 10.1046/j.1365-2516.1999.0050s1028.x]
- 41 **Wallny T**, Saker A, Hofmann P, Brackmann HH, Nicolay C, Kraft CN. Long-term follow-up after osteotomy for haemophilic arthropathy of the knee. *Haemophilia* 2003; **9**: 69-75 [PMID: 12558782 DOI: 10.1046/j.1365-2516.2003.00705.x]
- 42 **Mortazavi SM**, Heidari P, Esfandiari H, Motamedi M. Trapezoid supracondylar femoral extension osteotomy for knee flexion contractures in patients with haemophilia. *Haemophilia* 2008; **14**: 85-90 [PMID: 18005146]
- 43 **Sheth DS**, Oldfield D, Ambrose C, Clyburn T. Total knee arthroplasty in hemophilic arthropathy. *J Arthroplasty* 2004; **19**: 56-60 [PMID: 14716652 DOI: 10.1016/j.arth.2003.08.008]
- 44 **Rodriguez-Merchan EC**, Luck JV Jr, Silva M, Riera JA, Wiedel JD, Goddard NJ, Heim M, Solimeno PL. Total knee replacement in the haemophilic patient. In: *The Haemophilic Joints.-New Perspectives*. Rodriguez-Merchan EC, editor. Blackwell Publishing, Oxford, 2003: 116-124 [DOI: 10.1002/9780470986929.ch21]
- 45 **Norian JM**, Ries MD, Karp S, Hambleton J. Total knee arthroplasty in hemophilic arthropathy. *J Bone Joint Surg Am* 2002; **84-A**: 1138-1141 [PMID: 12107312]
- 46 **Ragni MV**, Crossett LS, Herndon JH. Postoperative infection following orthopaedic surgery in human immunodeficiency virus-infected hemophiliacs with CD4 counts $\leq 200/\text{mm}^3$. *J Arthroplasty* 1995; **10**: 716-721 [PMID: 8749751 DOI: 10.1016/S0883-5403(05)80065-8]
- 47 **Rodriguez-Merchan EC**. Total knee arthroplasty in patients with haemophilia who are HIV-positive. *J Bone Joint Surg Br* 2002; **84**: 170-172 [PMID: 11922355 DOI: 10.1302/0301-620X.84B2.13015]
- 48 **Powell DL**, Whitener CJ, Dye CE, Ballard JO, Shaffer ML, Eyster ME. Knee and hip arthroplasty infection rates in persons with haemophilia: a 27 year single center experience during the HIV epidemic. *Haemophilia* 2005; **11**: 233-239 [PMID: 15876268 DOI: 10.1111/j.1365-2516.2005.01081.x]
- 49 **Rodriguez-Merchán EC**. Total Knee Arthroplasty in Hemophilic Arthropathy. *Am J Orthop (Belle Mead NJ)* 2015; **44**: E503-E507 [PMID: 26665252]
- 50 **Jimenez-Yuste V**, Rodriguez-Merchan EC, Alvarez-Roman MT, Martin-Salces M. Hematological concepts and hematological perioperative treatment. In: *Joint Surgery in the Adult Patient with Hemophilia*. Rodriguez-Merchan EC, editor. Springer International Publishing Switzerland, 2015: 13-19 [DOI: 10.1007/978-3-319-10780-6_2]
- 51 **Wong JM**, Mann HA, Goddard NJ. Perioperative clotting factor replacement and infection in total knee arthroplasty. *Haemophilia* 2012; **18**: 607-612 [PMID: 22188657 DOI: 10.1111/j.1365-2516.2011.02728.x]
- 52 **Martinowitz U**, Schulman S, Gitel S, Horozowski H, Heim M, Varon D. Adjusted dose continuous infusion of factor VIII in patients with haemophilia A. *Br J Haematol* 1992; **82**: 729-734 [PMID: 1482660 DOI: 10.1111/j.1365-2141.1992.tb06951.x]
- 53 **Batorova A**, Martinowitz U. Intermittent injections vs. continuous infusion of factor VIII in haemophilia patients undergoing major surgery. *Br J Haematol* 2000; **110**: 715-720 [PMID: 10997985 DOI: 10.1046/j.1365-2141.2000.02226.x]
- 54 **Jiménez-Yuste V**, Rodriguez-Merchan EC, Alvarez MT, Quintana M, Fernandez I, Hernandez-Navarro F. Controversies and challenges in elective orthopedic surgery in patients with hemophilia and inhibitors. *Semin Hematol* 2008; **45**: S64-S67 [PMID: 18544428 DOI: 10.1053/j.seminhematol.2008.03.009]
- 55 **Stephensen D**. Rehabilitation of patients with haemophilia after orthopaedic surgery: a case study. *Haemophilia* 2005; **11** Suppl 1: 26-29 [PMID: 16219047 DOI: 10.1111/j.1365-2516.2005.01151.x]
- 56 **De la Corte-Rodriguez H**, Rodriguez-Merchan EC. The role of

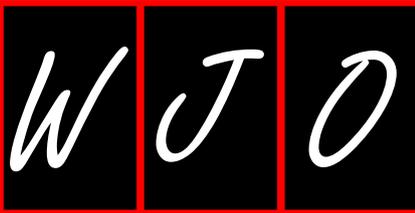
physical medicine and rehabilitation in haemophilic patients. *Blood Coagul Fibrinolysis* 2013; **24**: 1-9 [PMID: 23103725 DOI: 10.1097/MBC.0b013e32835a72f3]

57 **Rodriguez-Merchan EC**, Rocino A, Ewenstein B, Bartha L, Batorova A, Goudemand J, Gringeri A, Joao-Diniz M, Lopaciuk

S, Negrier C, Quintana M, Tagariello G, Tjonnnfjord GE, Villar VA, Vorlova Z. Consensus perspectives on surgery in haemophilia patients with inhibitors: summary statement. *Haemophilia* 2004; **10** Suppl 2: 50-52 [PMID: 15385047 DOI: 10.1111/j.1365-2516.2004.00933.x]

P- Reviewer: Ohishi T, Samulski RJ, Zak L
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D





Retrospective Study

Joint arthroplasty Perioperative Surgical Home: Impact of patient characteristics on postoperative outcomes

Duy L Phan, Kyle Ahn, Joseph B Rinehart, Michael-David Calderon, Wei-Der Wu, Ran Schwarzkopf

Duy L Phan, Department of Orthopaedic Surgery, University of California, Irvine Medical Center, Orange, CA 92868, United States

Kyle Ahn, Joseph B Rinehart, Michael-David Calderon, Wei-Der Wu, Department of Anesthesiology, University of California, Irvine Medical Center, Orange, CA 92868, United States

Ran Schwarzkopf, Division of Adult Reconstruction, Department of Orthopaedic Surgery, New York University Langone Medical Center, New York, NY 10279, United States

Author contributions: Phan DL wrote and revised the manuscript; Ahn K and Schwarzkopf R designed the research study, performed data collection and revised the manuscript; Rinehart JB designed the research study, performed data collection and statistical analysis, and revised the manuscript; Calderon MD and Wu WD performed data collection and statistical analysis.

Institutional review board statement: The study was reviewed and approved by the University of California, Irvine Institutional Review Board.

Informed consent statement: Informed consent was waived by the IRB.

Conflict-of-interest statement: Dr. Phan has no relevant disclosures to make in relation to the submitted study. Dr. Phan has not received research funding, speaker fees, consulting fees, or royalties from any organizations. Dr. Phan is an employee of the Department of Orthopaedic Surgery, University of California, Irvine Medical Center. Dr. Phan does not own company stock or options. Dr. Phan does not own any patents. Dr. Phan is not on the editorial board of any journals. Dr. Phan is not a board member of any societies. Dr. Schwarzkopf has a conflict of interest with Smith&Nephew, Intelijoint, Gauss Surgical.

Data sharing statement: All technical data is available from the corresponding author at schwarzk@gmail.com. Consent was not obtained for data sharing but the presented data is anonymized and the risk of identification is low.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative

Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Ran Schwarzkopf, MD, MSc, Assistant Professor, Division of Adult Reconstruction, Department of Orthopaedic Surgery, New York University Langone Medical Center, 301 East 17th Street, New York, NY 10279, United States. schwarzk@gmail.com
Telephone: +1-212-5137711

Received: February 10, 2016
Peer-review started: February 14, 2016
First decision: March 1, 2016
Revised: March 7, 2016
Accepted: March 24, 2016
Article in press: March 25, 2016
Published online: June 18, 2016

Abstract

AIM: To determine the impact of different characteristics on postoperative outcomes for patients in a joint arthroplasty Perioperative Surgical Home (PSH) program.

METHODS: A retrospective review was performed for patients enrolled in a joint arthroplasty PSH program who had undergone primary total hip arthroplasty (THA) and total knee arthroplasty (TKA). Patients were preoperatively stratified based on specific procedure performed, age, gender, body mass index (BMI), American Society of Anesthesiologists Physical Classification System (ASA) score, and Charleston Comorbidity Index (CCI) score. The primary outcome criterion was hospital length of stay (LOS). Secondary criteria including operative room (OR) duration, trans-

fusion rate, Post-Anesthesia Care Unit (PACU) stay, readmission rate, post-operative complications, and discharge disposition. For each outcome, the predictor variables were entered into a generalized linear model with appropriate response and assessed for predictive relationship to the dependent variable. Significance level was set to 0.05.

RESULTS: A total of 337 patients, 200 in the TKA cohort and 137 in the THA cohort, were eligible for the study. Nearly two-third of patients were female. Patient age averaged 64 years and preoperative BMI averaged 29 kg/m². The majority of patients were ASA score III and CCI score 0. After analysis, ASA score was the only variable predictive for LOS ($P = 0.0011$) and each increase in ASA score above 2 increased LOS by approximately 0.5 d. ASA score was also the only variable predictive for readmission rate ($P = 0.0332$). BMI was the only variable predictive for PACU duration ($P = 0.0136$). Specific procedure performed, age, gender, and CCI score were not predictive for any of the outcome criteria. OR duration, transfusion rate, post-operative complications or discharge disposition were not significantly associated with any of the predictor variables.

CONCLUSION: The joint arthroplasty PSH model reduces postoperative outcome variability for patients with different preoperative characteristics and medical comorbidities.

Key words: Perioperative Surgical Home; Arthroplasty; Length of stay; American Society of Anesthesiologists Physical Classification System; Body mass index

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The Perioperative Surgical Home (PSH) model is designed to improve healthcare delivery and reduce medical costs. In this study, patients in a joint arthroplasty PSH program were stratified based on preoperative characteristics and comorbidities to determine if these variables would impact postoperative results. Our results suggest that a joint arthroplasty PSH program may improve postoperative consistency and limit the influence of different patient attributes on surgical outcome. Arthroplasty patients with preoperative characteristics traditionally considered risk factors for negative outcomes, such as a high body mass index or an elderly age, may benefit from enrollment in a PSH program.

Phan DL, Ahn K, Rinehart JB, Calderon MD, Wu WD, Schwarzkopf R. Joint arthroplasty Perioperative Surgical Home: Impact of patient characteristics on postoperative outcomes. *World J Orthop* 2016; 7(6): 376-382 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/376.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.376>

INTRODUCTION

The relative increase in the elderly population, combined with changing indications for younger patients, is predicted to result in a growing number of patients undergoing total joint arthroplasty (TJA)^[1-3]. This will likely result in a diverse surgical population, with different medical comorbidities and characteristics, which can potentially lead to equally variable results. Standardizing and streamlining the operative experience and minimizing procedural and patient variables will thus be essential to ensure optimal and predictable outcomes.

The Perioperative Surgical Home (PSH) has been promoted as a patient-centered model to improve health, healthcare delivery, and reduce medical costs^[4-6]. A multidisciplinary team led by the primary surgeon and anesthesiologist engages with the patient, starting from the moment the decision for surgery is made all the way through to the post-operative 30-d recovery phase, to yield the best possible results and optimize value for both the patient and the healthcare system. PSH is ideally designed to enhance the perioperative experience, regardless of preoperative patient conditions, and has been implemented in different patient populations with beneficial results^[7].

The purpose of this study was to examine the results of a TJA PSH protocol designed and adopted at our institution. Preoperative stratification and postoperative outcomes for patients undergoing primary total knee (TKA) and primary total hip (THA) arthroplasty were analyzed to determine the effects of PSH. Our hypothesis was that the joint arthroplasty PSH will lead to equivalent or improved perioperative outcomes regardless of our patients' preoperative comorbidity burden.

MATERIALS AND METHODS

After institutional review board approval was obtained, a retrospective review was performed of joint arthroplasty PSH patients undergoing elective primary TKA and THA at our institution from October 2012 through February 2015. The structure of the PSH protocol is detailed in Figure 1. All surgeries were performed by the senior author. Exclusion criteria included revision, bilateral, and acute post-traumatic arthroplasty. During surgery, all TKA patients were supine and underwent a medial parapatellar approach with the use of a tourniquet, while THA patients were lateral decubitus and underwent either a posterolateral or modified lateral surgical approach.

Patient charts were pulled from the PSH data mart for analysis. Preoperative variables that were stratified included: Specific procedure, age, gender, body mass index (BMI), Charleston Comorbidity Index (CCI), and American Society of Anesthesiologists Physical Classification System score (ASA). The primary outcome criteria measured was length of stay (LOS); secondary outcomes included operating room (OR) duration, trans-

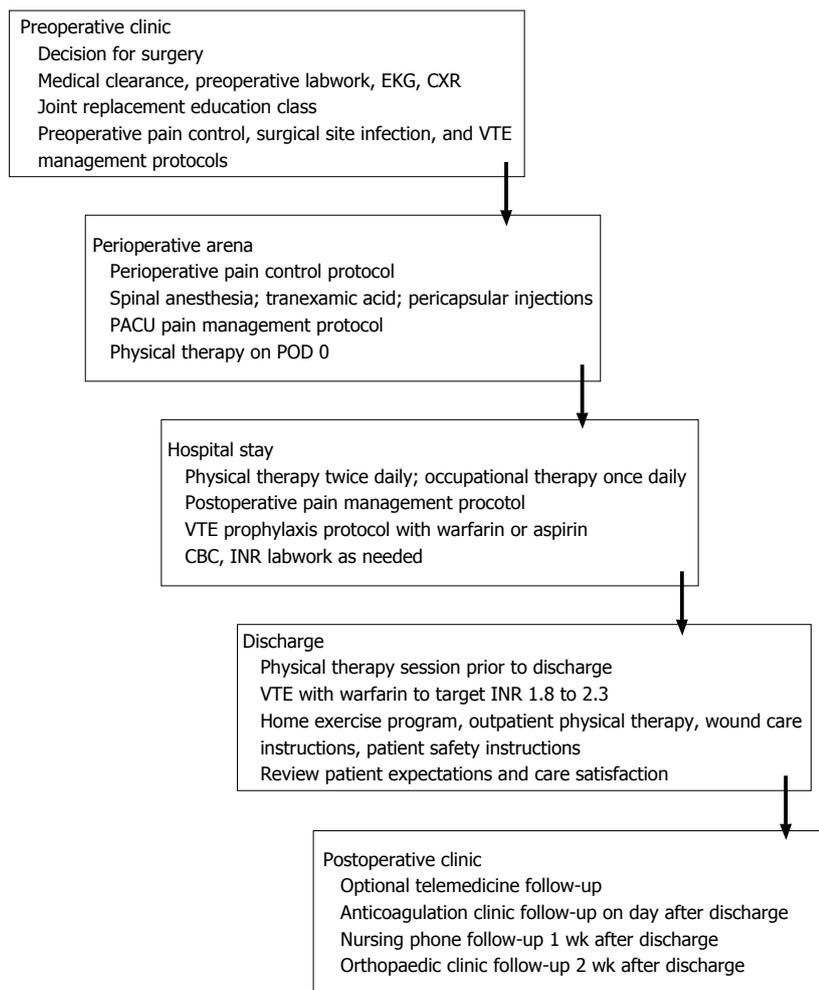


Figure 1 Total joint arthroplasty Perioperative Surgical Home protocol. PACU: Post-anesthesia care unit; EKG: Electrocardiogram; CXR: Chest X-ray; VTE: Venous thromboembolism; POD: Postoperative day; CBC: Complete blood count.

fusion rate, Post-Anesthesia Care Unit (PACU) stay, readmission rate, post-operative complications, and discharge disposition up to 30-d post-surgery.

Statistical analysis

For the primary and secondary outcomes, the predictor variables were entered into a generalized linear model with appropriate response (Linear for scalar measures, Gamma for counts or time, logit for binary outcomes like readmissions) and assessed for predictive relationship to the dependent variable. Significance level was set to 0.01 to correct for multiple comparisons. Demographics and variable summaries were presented as mean ± SD, or as percentage for binary outcomes. Statistics were performed with Microsoft Excel (Microsoft, Redmond, WA); SPSS (IBM, Armonk NY), and R (R-Project, <https://www.r-project.org/>).

RESULTS

Our cohort included 337 patients, 200 undergoing TKA and 137 undergoing THA. The average age was slightly over 60 years of age and almost two-thirds of patients were female. The most common preoperative medical

comorbidity was hypertension, while the majority of patients were rated as ASA III and CCI 0 when evaluating for overall medical condition. Complete patient demographics are shown in Table 1. The average total OR time was slightly over three hours and the average PACU stay was slightly over two hours. The average hospital length of stay was two and a half days. The rate of hospital readmission was minimal. Complete surgical outcomes are shown in Table 2.

With regards to the primary outcome, age, BMI, and ASA score were all predictive of LOS. Specific procedure performed, gender, and CCI scores were non-significant. ASA score was strongly predictive of LOS ($P = 0.0011$) as shown in Figure 2; on average each increase in ASA score above 2 increased LOS by 0.5 d. Age was only weakly predictive ($P = 0.0021$), with older patients having a slightly shorter LOS. Similarly, BMI was weakly predictive ($P = 0.0003$), with higher BMI patients having slightly shorter LOS.

With regards to secondary outcomes, ASA score was the only variable predictive of readmission rate ($P = 0.0332$). With a 0.6% readmission rate, however, the power for this outcome was low. BMI was the only variable predictive of increased PACU duration ($P =$

Table 1 Patient demographics and comorbidities

Number	337
Age (yr)	63.7 ± 13.8
Gender (M/F)	123/214
Procedure (THA/TKA)	137/200
BMI (kg/m ²)	29.4 ± 6.2
Congestive heart failure	6 (1.8%)
Chronic obstructive pulmonary disease	25 (7.4%)
Diabetes mellitus	59 (17.5%)
Hypertension	198 (58.8%)
History of myocardial infarction	17 (5.0%)
American Society of Anesthesiologist score	I -0 (0.0%)
	II -67 (19.9%)
	III -255 (75.7%)
	IV -15 (4.5%)
Charlson Comorbidity Index score	0-226 (67.1%)
	1-85 (25.2%)
	2-24 (7.1%)
	6-2 (0.6%)

THA: Total hip arthroplasty; TKA: Total knee arthroplasty; BMI: Body mass index; M: Male; F: Female.

Table 2 Surgical outcomes

OR duration (min)	189 ± 60
PACU duration (min)	138 ± 80
Transfusion rate	32 (9.5%)
Length of stay (d)	2.5 ± 0.8
Severe postoperative nausea and vomiting	15 (4.5%)
Emergency department visits	7 (2.1%)
Readmissions	2 (0.6%)

PACU: Post-anesthesia care unit; OR: Operative room.

0.0136), with higher BMI leading to slightly longer PACU stay. Specific procedure performed, age, gender, and CCI score were not predictive for any of the secondary outcome criteria. OR duration, transfusion rate, post-operative complications or discharge disposition were not significantly associated with any of the predictor variables.

DISCUSSION

TKA and THA are common orthopaedic procedures that provide reliable and beneficial outcomes for the majority of patients^[8,9]. However, despite advancements in surgical implants, technique, and management, a minority of patients continue to do comparatively poorly^[10,11]. The expected significant increase in the patient population eligible for TJA will only increase the overall number of patients that have suboptimal outcomes. The goal of this study was to examine if TJA patients, managed under a new surgical home care model, perioperative outcomes were equivalent or better as compared to national standards.

The PSH has been endorsed by the American Society of Anesthesiologists as a model to decrease the variability in perioperative care^[4]. PSH starts in the office, where immediately after a decision for surgery is made,

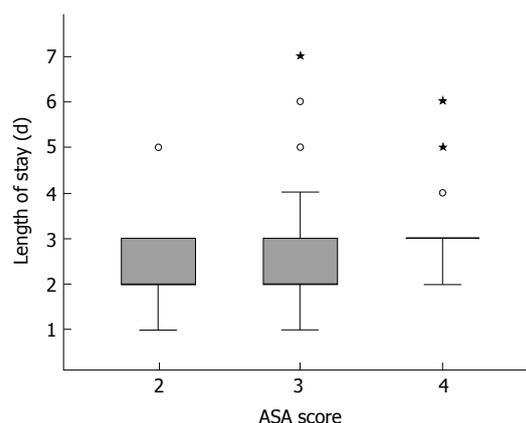


Figure 2 Box plots showing American Society of Anesthesiologists score was strongly predictive of length of stay ($P = 0.0011$) as shown in the figure; on average each increase in American Society of Anesthesiologists score above 2 increased length of stay by 0.5 d.

both surgical and anesthesiology teams are in constant communication with the patient. Perioperative factors such as surgical technique, anesthetic delivery, pain control, and discharge disposition are addressed to help formulate an operative plan and set expectations. During surgery, perioperative variables are minimized due to consistent protocol based surgical and anesthesiology performance; potential pitfalls are avoided by adhering to the operative plan and perioperative pathways and deviating only when necessary. After surgery, dedicated inpatient ancillary staff, including nurses and therapists, assist the surgical and anesthesiology teams to provide a smooth transition to discharge. Patients follow-up with the surgical and anesthesiology teams to ensure postoperative continuity of care. By having a patient-centered team assuring continuity of care throughout the surgical period and applying evidence-based medicine in a consistent and standardized manner, PSH is designed to minimize errors, reduce unnecessary costs, and improve patient outcomes. Studies examining the benefits of PSH are currently limited, likely due to only a recent increase in popularity. However, PSH has been implemented in cardiac and vascular patients^[12] as well as in a Veterans Affairs population^[13] with success, and results are expected to be forthcoming as more institutions adopt the PSH model.

In the current orthopaedic literature, only 2 significant studies have been published analyzing patients in a PSH model. Boraiah *et al*^[14] recently published a study examining the utility of a scoring system, the Readmission Risk Assessment Tool, for TJA patients in their PSH model and noted that preoperative patient stratification could predict readmission rates. However, the benefits of PSH on patient outcomes were not directly examined. The results of PSH implementation have recently been published after adoption of a TJA protocol at our institution, with postoperative outcome measures comparable to national benchmarks^[6]. However, this study did not stratify patients preoperatively to determine if the outcomes were due to PSH or if there was an

inherent selection bias that played a role. The current study is a follow-up to that first initial analysis to examine if the benefits of the PSH model could be isolated and specified, and to predict if similar outcomes could be achieved among patients with a differing preoperative comorbidity burden.

Preoperative stratification took into account different variables, all of which have been examined previously in the literature. An increased patient age has been shown to result in higher hospital LOS^[15-17], readmission rates^[15,18-20], increased complication rate^[16,21,22], and disposition to an extended care facility^[16]. Interestingly, a relatively young age at time of surgery has also been shown to increase readmission rates^[11,20]. Male gender resulted in a higher readmission rate in most studies^[11,19,23,24] while female gender was the predictor of readmission in another^[25], and associated with a longer LOS^[26]. Male gender also predicted a higher complication rate^[24]. Obesity resulted in a longer hospital LOS^[17,27,28], readmission rate^[19,20,23,27], and complication rate^[21,22,28]. An underweight status has also been shown to increase the rate of readmission^[20]. A higher ASA score predicted a longer LOS^[26], higher rate of readmission^[23,25,29], and complication rate^[29]. A higher CCI score predicted higher rate of readmission^[30] and a higher complication rate^[31].

In the current study, the influence of preoperative variables appeared to be minimized as patients underwent TJA in a PSH care model. As contrasted to the previously mentioned studies, patient gender, procedure type, and CCI score did not have any significant correlation with peri-operative outcome criteria, including LOS, PACU duration, discharge disposition, complication rate, and readmission rate. This does not imply that these variables do not play a role in patient outcomes. Rather, it suggests that within a PSH care model, the effects of these variables on the outcomes in TJA patients are reduced. This is likely due to standardization of the entire continuum of perioperative care that includes close follow-up of patients by a dedicated PSH team, and incorporation of evidence-based clinical pathways. These processes help reduce the variability in the delivery and quality of care typically found within a traditional care model. The effect of age was also diminished. Similarly, preoperative BMI also had a diminished effect with outcome criteria, aside from PACU duration.

The effects of both age and BMI on LOS, while very weak, were the opposite of what has been previously reported in other studies (both increasing age and BMI led to marginally but statistically significant shorter LOS). We hypothesize that this may be because younger, thinner patients who are having total joint replacements are more likely to have other physical or social factors contributing to their need for replacement which may contribute to longer LOS (for example narcotic dependence), as opposed to older or heavier patients who are more likely to have uncomplicated primary osteoarthritis joint degeneration.

Higher ASA scores were strongly predictive for an increase in hospital LOS, with each point increase above

2 resulting in an increased stay of 0.5 d. Similarly, higher ASA scores were strongly predictive for patient readmission rates. There was not a strong correlation between ASA scores and other outcome criteria, which is surprising because a large number of readmissions are due to post-operative complications. Also surprising is that CCI scoring did not result in a similar correlation to LOS and readmission rates. Like the ASA model, CCI is designed to evaluate overall patient comorbidity and as such it would be expected that stratification of both would lead to comparable outcomes. It is possible that the ASA score intrinsically includes the information contained in CCI such that using both in the same model becomes redundant. The ASA score is also more discriminating between the full range of mild to severe comorbidity, whereas the CCI tends to discriminate better between moderate and severe comorbidity only.

There were several limitations to the study that may have affected the results. The study was retrospective in nature, which may have led to inadvertent biases. However, preoperative exclusion criteria and stratification was stringently designed in order to limit any bias. The surgeries were all performed by one surgeon, which may have skewed outcomes but also limited surgical variation. This was supported by using standard surgical approaches and the same implant system for all patients. Although samples sizes were not small, a larger patient population would have increased the power of the study. Patient outcomes were included only up to the 30-d postoperative period and changes afterwards were not incorporated into outcome analysis. Finally, patients readmitted elsewhere would not have been captured within our study, although such a limitation is not unique to our study. Our joint replacement PSH was designed to encompass perioperative patient care up to 30-d after surgery; as such we felt it appropriate to end data collection at this time point.

The PSH is a patient-centered care model designed to provide coordinated care through shared decision-making and standardization using evidence-based medicine. Through physician-led multidisciplinary care, this care model aims to add value and help achieve Institute for Healthcare's Triple Aim of improving patient-care experience and population health at a reduced cost. Our study suggests that patient factors, which have historically influenced TJA results, such as age, gender, CCI scores, and BMI, may be minimized. To the best of our knowledge, this is the first study examining the outcomes of TJA patients in a PSH model. Further prospective studies are needed in order to support our results.

COMMENTS

Background

Perioperative Surgical Home (PSH) is a patient-centered program designed to improve clinical efficiency, optimize surgical results, and decrease the financial burden on healthcare. The increasing number of patients who will undergo total joint arthroplasty (TJA) makes this subset of the medical population ideal for enrollment in a PSH protocol.

Research frontiers

PSH has been used selectively with beneficial results in different patient populations in the last decade. Optimizing patient outcome after TJA has been a focus of analysis since these surgeries were invented and recent studies have highlighted different factors, such as age, weight, gender, and procedure performed, that have an influence on outcomes.

Innovations and breakthroughs

To our knowledge, this study is the first of its kind stratifying TJA PSH patients preoperatively based on different characteristics and comorbidities and identifying associations with postoperative outcomes. The results suggest that a majority of patients with different preoperative variables may have equivalent outcomes due to perioperative optimization in a PSH protocol.

Applications

The study shows the efficacy and safety for TJA patients enrolled in a PSH protocol and suggests that preoperative differences may be minimized through this patient-centered model.

Terminology

PSH: Patient-centered multidisciplinary team led by the lead surgeon and anesthesiologist.

Peer-review

The manuscript is well written and the use of English is good.

REFERENCES

- Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89**: 780-785 [PMID: 17403800]
- Kurtz SM, Ong KL, Lau E, Bozic KJ. Impact of the economic downturn on total joint replacement demand in the United States: updated projections to 2021. *J Bone Joint Surg Am* 2014; **96**: 624-630 [PMID: 24740658 DOI: 10.2106/JBJS.M.00285]
- Ravi B, Croxford R, Reichmann WM, Losina E, Katz JN, Hawker GA. The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007. *Best Pract Res Clin Rheumatol* 2012; **26**: 637-647 [PMID: 23218428 DOI: 10.1016/j.berh.2012.07.014]
- Cannesson M, Kain Z. The perioperative surgical home: an innovative clinical care delivery model. *J Clin Anesth* 2015; **27**: 185-187 [PMID: 25704673 DOI: 10.1016/j.jclinane.2015.01.006]
- Desebbe O, Lanz T, Kain Z, Cannesson M. The perioperative surgical home: An innovative, patient-centred and cost-effective perioperative care model. *Anaesth Crit Care Pain Med* 2016; **35**: 59-66 [PMID: 26613678 DOI: 10.1016/j.accpm.2015.08.001]
- Garson L, Schwarzkopf R, Vakharia S, Alexander B, Stead S, Cannesson M, Kain Z. Implementation of a total joint replacement-focused perioperative surgical home: a management case report. *Anesth Analg* 2014; **118**: 1081-1089 [PMID: 24781576 DOI: 10.1213/ANE.0000000000000191]
- Kash BA, Zhang Y, Cline KM, Menser T, Miller TR. The perioperative surgical home (PSH): a comprehensive review of US and non-US studies shows predominantly positive quality and cost outcomes. *Milbank Q* 2014; **92**: 796-821 [PMID: 25492605 DOI: 10.1111/1468-0009.12093]
- Learmonth ID, Young C, Rorabeck C. The operation of the century: total hip replacement. *Lancet* 2007; **370**: 1508-1519 [PMID: 17964352]
- Kane RL, Saleh KJ, Wilt TJ, Bershadsky B. The functional outcomes of total knee arthroplasty. *J Bone Joint Surg Am* 2005; **87**: 1719-1724 [PMID: 16085610]
- Pulido L, Parvizi J, Macgibeny M, Sharkey PF, Purtill JJ, Rothman RH, Hozack WJ. In hospital complications after total joint arthroplasty. *J Arthroplasty* 2008; **23**: 139-145 [PMID: 18722311 DOI: 10.1016/j.arth.2008.05.011]
- Zmistowski B, Restrepo C, Hess J, Adibi D, Cangoz S, Parvizi J. Unplanned readmission after total joint arthroplasty: rates, reasons, and risk factors. *J Bone Joint Surg Am* 2013; **95**: 1869-1876 [PMID: 24132361 DOI: 10.2106/JBJS.L.00679]
- Silvay G, Zafirova Z. Ten Years Experiences With Preoperative Evaluation Clinic for Day Admission Cardiac and Major Vascular Surgical Patients: Model for "Perioperative Anesthesia and Surgical Home". *Semin Cardiothorac Vasc Anesth* 2016; **20**: 120-132 [PMID: 26620138 DOI: 10.1177/1089253215619236]
- Walters TL, Howard SK, Kou A, Bertaccini EJ, Harrison TK, Kim TE, Shafer A, Brun C, Funck N, Siegel LC, Stary E, Mariano ER. Design and Implementation of a Perioperative Surgical Home at a Veterans Affairs Hospital. *Semin Cardiothorac Vasc Anesth* 2016; **20**: 133-140 [PMID: 26392388 DOI: 10.1177/1089253215607066]
- Boraiah S, Joo L, Inneh IA, Rathod P, Meftah M, Band P, Bosco JA, Iorio R. Management of Modifiable Risk Factors Prior to Primary Hip and Knee Arthroplasty: A Readmission Risk Assessment Tool. *J Bone Joint Surg Am* 2015; **97**: 1921-1928 [PMID: 26631992 DOI: 10.2106/JBJS.N.01196]
- Jauregui JJ, Boylan MR, Kapadia BH, Naziri Q, Maheshwari AV, Mont MA. Total Joint Arthroplasty in Nonagenarians: What Are the Risks? *J Arthroplasty* 2015; **30**: 2102-2105.e1 [PMID: 26169454 DOI: 10.1016/j.arth.2015.06.028]
- Fang M, Noiseux N, Linson E, Cram P. The Effect of Advancing Age on Total Joint Replacement Outcomes. *Geriatr Orthop Surg Rehabil* 2015; **6**: 173-179 [PMID: 26328232 DOI: 10.1177/2151458515583515]
- Bradley BM, Griffiths SN, Stewart KJ, Higgins GA, Hockings M, Isaac DL. The effect of obesity and increasing age on operative time and length of stay in primary hip and knee arthroplasty. *J Arthroplasty* 2014; **29**: 1906-1910 [PMID: 25081514 DOI: 10.1016/j.arth.2014.06.002]
- Avram V, Petruccioli D, Winemaker M, de Beer J. Total joint arthroplasty readmission rates and reasons for 30-day hospital readmission. *J Arthroplasty* 2014; **29**: 465-468 [PMID: 23993434 DOI: 10.1016/j.arth.2013.07.039]
- Paxton EW, Inacio MC, Singh JA, Love R, Bini SA, Namba RS. Are There Modifiable Risk Factors for Hospital Readmission After Total Hip Arthroplasty in a US Healthcare System? *Clin Orthop Relat Res* 2015; **473**: 3446-3455 [PMID: 25845947 DOI: 10.1007/s11999-015-4278-x]
- Saucedo JM, Marecek GS, Wanke TR, Lee J, Stulberg SD, Puri L. Understanding readmission after primary total hip and knee arthroplasty: who's at risk? *J Arthroplasty* 2014; **29**: 256-260 [PMID: 23958236 DOI: 10.1016/j.arth.2013.06.003]
- Belmont PJ, Goodman GP, Hamilton W, Waterman BR, Bader JO, Schoenfeld AJ. Morbidity and mortality in the thirty-day period following total hip arthroplasty: risk factors and incidence. *J Arthroplasty* 2014; **29**: 2025-2030 [PMID: 24973000 DOI: 10.1016/j.arth.2014.05.015]
- Belmont PJ, Goodman GP, Waterman BR, Bader JO, Schoenfeld AJ. Thirty-day postoperative complications and mortality following total knee arthroplasty: incidence and risk factors among a national sample of 15,321 patients. *J Bone Joint Surg Am* 2014; **96**: 20-26 [PMID: 24382720 DOI: 10.2106/JBJS.M.00018]
- Pugely AJ, Callaghan JJ, Martin CT, Cram P, Gao Y. Incidence of and risk factors for 30-day readmission following elective primary total joint arthroplasty: analysis from the ACS-NSQIP. *J Arthroplasty* 2013; **28**: 1499-1504 [PMID: 23891054 DOI: 10.1016/j.arth.2013.06.032]
- Singh JA, Kwok CK, Richardson D, Chen W, Ibrahim SA. Sex and surgical outcomes and mortality after primary total knee arthroplasty: a risk-adjusted analysis. *Arthritis Care Res (Hoboken)* 2013; **65**: 1095-1102 [PMID: 23335560 DOI: 10.1002/acr.21953]
- Tayne S, Merrill CA, Smith EL, Mackey WC. Predictive risk factors for 30-day readmissions following primary total joint arthroplasty and modification of patient management. *J Arthroplasty* 2014; **29**: 1938-1942 [PMID: 24975486 DOI: 10.1016/j.arth.2014.05.023]
- Husted H, Holm G, Jacobsen S. Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-

- track experience in 712 patients. *Acta Orthop* 2008; **79**: 168-173 [PMID: 18484241 DOI: 10.1080/17453670710014941]
- 27 **Schwarzkopf R**, Thompson SL, Adwar SJ, Liublinska V, Slover JD. Postoperative complication rates in the “super-obese” hip and knee arthroplasty population. *J Arthroplasty* 2012; **27**: 397-401 [PMID: 21676578 DOI: 10.1016/j.arth.2011.04.017]
- 28 **Alvi HM**, Mednick RE, Krishnan V, Kwasny MJ, Beal MD, Manning DW. The Effect of BMI on 30 Day Outcomes Following Total Joint Arthroplasty. *J Arthroplasty* 2015; **30**: 1113-1117 [PMID: 25683294 DOI: 10.1016/j.arth.2015.01.049]
- 29 **Schaeffer JF**, Scott DJ, Godin JA, Attarian DE, Wellman SS, Mather RC. The Association of ASA Class on Total Knee and Total Hip Arthroplasty Readmission Rates in an Academic Hospital. *J Arthroplasty* 2015; **30**: 723-727 [PMID: 25575729 DOI: 10.1016/j.arth.2014.12.014]
- 30 **Mesko NW**, Bachmann KR, Kovacevic D, LoGrasso ME, O’Rourke C, Froimson MI. Thirty-day readmission following total hip and knee arthroplasty - a preliminary single institution predictive model. *J Arthroplasty* 2014; **29**: 1532-1538 [PMID: 24703364 DOI: 10.1016/j.arth.2014.02.030]
- 31 **Rasouli MR**, Restrepo C, Maltenfort MG, Purtill JJ, Parvizi J. Risk factors for surgical site infection following total joint arthroplasty. *J Bone Joint Surg Am* 2014; **96**: e158 [PMID: 25232088 DOI: 10.2106/JBJS.M.01363]

P- Reviewer: Malik H, Willis-Owen CA
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Observational Study

Quantifying prosthetic gait deviation using simple outcome measures

Lauren Kark, Ross Odell, Andrew S McIntosh, Anne Simmons

Lauren Kark, Ross Odell, Anne Simmons, Graduate School of Biomedical Engineering, University of New South Wales, Sydney, NSW 2052, Australia

Andrew S McIntosh, Australian Centre for Research into Injury in Sport and its Prevention, Federation University, Ballarat, Victoria 3350, Australia

Author contributions: All authors contributed equally to the design of the study; Kark L collected and analysed the data, and prepared the initial manuscript; data analysis was performed in collaboration with Odell R; all authors revised the article.

Institutional review board statement: This study received approval from the University of New South Wales Human Research Ethics Committee (approval No.: HREC07247).

Informed consent statement: All study participants provided informed written consent prior to study enrolment.

Conflict-of-interest statement: The authors report no conflicts of interest.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Lauren Kark, Graduate School of Biomedical Engineering, University of New South Wales, Samuels Building (F25), Gate 11 Botany Street, Randwick, Sydney, NSW 2052, Australia. lauren.kark@unsw.edu.au
Telephone: +61-2-93850560
Fax: +61-2-96632108

Received: January 29, 2016

Peer-review started: February 1, 2016

First decision: March 25, 2016

Revised: April 12, 2016

Accepted: May 7, 2016

Article in press: May 9, 2016

Published online: June 18, 2016

Abstract

AIM: To develop a subset of simple outcome measures to quantify prosthetic gait deviation without needing three-dimensional gait analysis (3DGA).

METHODS: Eight unilateral, transfemoral amputees and 12 unilateral, transtibial amputees were recruited. Twenty-eight able-bodied controls were recruited. All participants underwent 3DGA, the timed-up-and-go test and the six-minute walk test (6MWT). The lower-limb amputees also completed the Prosthesis Evaluation Questionnaire. Results from 3DGA were summarised using the gait deviation index (GDI), which was subsequently regressed, using stepwise regression, against the other measures.

RESULTS: Step-length (SL), self-selected walking speed (SSWS) and the distance walked during the 6MWT (6MWD) were significantly correlated with GDI. The 6MWD was the strongest, single predictor of the GDI, followed by SL and SSWS. The predictive ability of the regression equations were improved following inclusion of self-report data related to mobility and prosthetic utility.

CONCLUSION: This study offers a practicable alternative to quantifying kinematic deviation without the need to conduct complete 3DGA.

Key words: Gait deviation; Prosthesis; Amputation;

Functional outcomes; Regression; Receiver operating characteristic curve

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The number of available outcome measures and multi-dimensionality of functional status complicate appropriate selection. This study assists clinicians in choosing apposite measures by exploring the relationship between various measures and demonstrating that often expensive and unavailable measures can be estimated using a combination of readily available self-report and performance-based measures.

Kark L, Odell R, McIntosh AS, Simmons A. Quantifying prosthetic gait deviation using simple outcome measures. *World J Orthop* 2016; 7(6): 383-391 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/383.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.383>

INTRODUCTION

The multitude of available outcome measures and the multi-dimensional concept of functional status complicate the selection of appropriate outcome measures for use with lower-limb amputees (LLAs).

Numerous outcome measures are used with LLAs^[1], and are generally classified as either self-report or performance-based. Self-report measures have been used in abundance with lower limb amputees and include the generic short-form 36^[2] and amputee-specific prosthesis evaluation questionnaire (PEQ)^[3]. Ease of administration make self-report measures attractive clinical tools, but answers are highly subjective and affected by a multitude of factors^[4]. But, they provide a patient perspective, which in itself is an important part of functional status. Self-report measures also involve the patient in the decision-making process, which has been associated with improved patient outcome^[5]. More objective than self-report measures are performance-based measures, which assess the ability to perform everyday tasks. These can be divided into clinical- or laboratory-based and real-world measures^[6]. In contrast to self-report and real-world measures (for example, step-counters and accelerometers), which account for real-world experiences over a period of time, laboratory-based measures assess performance on defined tasks in an artificial environment and within a limited time period. Examples of laboratory-based measures used with LLAs include walking tests, such as the six-minute walk test and tests involving sit-to-stand and turning, such as the timed-up-and-go test (TUGT)^[1]. Three-dimensional gait analysis (3DGA) is another such example. It is considered the assessment of choice for gait because it measures gait dynamics in detail with a high level of reliability^[7,8]. Its low level of use with the LLA population

has been attributed to its financial, personnel and time cost^[9].

The correlation between outcome measures, including 3DGA, remains relatively unknown, particularly within the LLA population. Research into older people found that gait speed predicted self-perceived physical functioning^[10], but the relationships between self-administered, interview-administered and performance-based measures was inconsistent and the strength of correlation ranged from weak to moderate^[11,12]. Amongst diabetics and LLAs, research has shown that self-reported activity levels do not correlate with performance-based measures^[6,13]. Relationships between 3DGA and other outcome measures have been investigated in the context of paediatric cerebral palsy, where gait analysis has demonstrated moderate to strong correlation with measures derived from observational gait analysis^[14-17] and parent-report measures^[18,19]. Gait velocity however was representative of functional capacity in children with cerebral palsy^[20]. Archer *et al.*^[21] investigated the relationship between clinical factors, such as range of motion and strength, and observed gait deviation following lower extremity trauma, however excluded LLAs. Establishing the correlation between these outcome measures is important in order to: Assist in the development of appropriate research methods; assist in the interpretation of research results; advocate for resources to develop assessment facilities; and, identify the most appropriate assessments for individuals and populations. This paper will help establish the utility of selected measures in predicting gait deviation and contribute to the selection in research and clinical applications of cost-effective alternatives to 3DGA for the lower limb amputee population.

The aims of this study were to examine correlations between a selection of common outcome measures used to assess gait deviation and function in individuals with LLA, and to quantify kinematic deviation using a subset of these common outcome measures. This study was designed with the premise that 3DGA is the "gold standard" for measuring gait pathology, and it was hypothesised that simple outcome measures can be used to quantify overall kinematic deviation.

MATERIALS AND METHODS

Participants

Ethics approval was obtained (University of New South Wales Human Research Ethics Committee, UNSW HREC 07247), and 20 unilateral LLAs and 28 able-bodied participants were recruited using direct mail to a number of support groups. Informed consent was obtained prior to participation in this study. Exclusion criteria for the LLA group included multiple amputations, upper limb amputations, amputations at a level other than transfemoral or transtibial, less than six months consistent prosthesis use, use of walking aids other than walking sticks, or cognitive disabilities. Able-bodied participants were included to create a normative

database similar in age and body mass index to the LLA group. The exclusion criterion for the able-bodied participants was known gait pathology. Individuals aged less than 18 years were excluded.

Procedure

Participants underwent 3DGA wearing their everyday prosthesis (with shoes) and using regular walking aids (if normally used) at UNSW's Gait and Biomechanics Laboratory using an eight-camera Vicon 612 motion capture system (Oxford Metrics). Initial contact was detected by one of two embedded force plates (Kistler) located at the midpoint of the 15-m walkway. Markers were placed according to a modified Helen Hayes marker set^[22] with additional markers placed over the anterior portion of the pelvis to address anterior pelvic marker dropout during the gait cycle^[23]. Participants were recorded at a comfortable self-selected walking speed (SSWS), and at least six successful trials were collected for each limb. Success was defined by a complete foot strike of at least one of the in-ground force plates.

Following 3DGA, participants completed two performance-based tests - TUGT and the 6MWT as described in the literature^[24,25]. Both measures have demonstrated validity for use with LLAs^[26,27]. Practices were permitted for the TUGT, which was conducted three times. Participants completed a self-report measure, the PEQ, in rest periods throughout the test protocol. Able-bodied participants underwent the same protocol, but did not complete the PEQ.

Statistical analysis

Lower limb kinematics and temporospatial data were calculated using the Plug-In-Gait model (Vicon, Oxford Metrics). Step-length (SL) and SSWS were normalised against average leg-length for each participant. Leg-length was defined as the distance between the anterior superior iliac spine and the medial malleolus on the same side, and the arithmetic mean of the left and right leg-length formed the average leg-length value used for normalisation. The gait deviation index (GDI) was calculated using the template provided by its authors^[28]. For the amputee group, the GDI was calculated for six trials per limb per participants and averaged to obtain the value used in subsequent analyses. A representative trial from the left and right limb was used from each able-bodied participant, and contributed to the normative database required for the calculation of the GDI. In doing so, the GDI distribution for the able-bodied participants has a mean value of 100, with every 10 points below equal to one standard deviation away from the mean. The average of the three TUGTs was used in further statistical analyses. The time taken to stand (t_{stand}) was derived from the TUGT. Both the summary scales and individual questions from the PEQ were utilised.

Normalcy of data was assessed using the Anderson-Darling test. Summary statistics were calculated using measures appropriate to their distribution - mean and standard deviation for normal distributions, and median

and interquartile range for non-normal distributions. Analysis of variance was used to compare results between the able-bodied group, transtibial amputee group and transfemoral amputee group for normally distributed data (Table 1). Kruskal-Wallis one-way analysis of variance was used for data that did not conform to a normal distribution. A P -value of less than 0.05 was considered significant.

Spearman's rank correlation coefficient, ρ , was used to determine the relationships between the GDI and participant characteristics, performance-based measures and self-report measures. Strict significant criteria for the correlation coefficient were required to minimise the chance of coincidental findings, possible due to the large number of relationships investigated in this study^[29]. Significance was set at $P \leq 0.001$, or $|\rho| \geq 0.70$.

Stepwise regression analyses were used to determine the major predictors of the GDI (dependent variable), with participant characteristics (as listed in Table 1 and including aetiology), performance-based measures and responses from the PEQ used as independent variables in the regression models. The alpha-to-enter and alpha-to-exclude were set to 0.2 to accommodate the small sample size^[30]. Predicted R^2 values were calculated using a leave one out cross-validation protocol. Three types of regression analyses were performed for various reasons. The GDI was the dependent variable in all models.

All independent variables: A purely explorative model, including all independent variables to determine the best possible predictors of the GDI.

Omission of SL relationships: Clinical utility requires that reliance on instrumentation be minimised. Of the outcome measures adopted in this study, with the exception of the GDI, instrumentation was required only for the calculation of SL. Other measures needed little more than a stopwatch to obtain. SL relationships were omitted from the second regression analysis to minimise the need for instrumentation and consider applicability.

Forced inclusion of walking speed relationships, omission of SL relationships: Walking speed is often considered a robust measure of functional ability^[1] in population groups with movement disorders. This was investigated in the final regression analysis by forcing the inclusion of walking speed relationships as independent variables.

Since frustration is known to affect self-efficacy^[31], responses to self-report measures will differ between participants reporting frustration and participants reporting an absence of frustration. The PEQ contains within it questions relating to frustration. To account for differences in self-efficacy, participants were separated based upon the presence ($n = 16$) and absence of frustration ($n = 4$) as measured by the frustration

Table 1 Summary of results

Participant characteristics	Summary statistic	Transtibial	Transfemoral	Able-bodied
Number	Count	12	8	28
Number of women	Count	3	3	16
Age (yr)	Mean (SD)	61.7 (12.6)	63.3 (12.0)	60.6 (7.8)
BMI (kg/m ²)	Mean (SD)	27.3 (6.5)	25.4 (4.4)	25.6 (3.1)
Age _{amp} (yr)	Mean (SD)	40.9 (19.2)	38.9 (23.0)	NA
Time (yr)	Median (IQR)	17.0 (27.3)	22.5 (38.5)	NA
Use (h/d)	Median (IQR)	15.5 (1.0)	13.0 (10.0)	NA
Performance-based outcomes				
GDI (-) ^a	Mean (SD)	81.2 (13.6)	68.8 (8.8)	NA
nSL (-) ^{a,b}	Mean (SD)	0.76 (0.11)	0.65 (0.10)	0.87 (0.06)
nSSWS (/s) ^{a,b}	Mean (SD)	1.36 (0.27)	1.01 (0.23)	1.72 (0.19)
TUGT (s) ^{a,b}	Median (IQR)	10.0 (2.0)	12.7 (7.5)	7.9 (1.4)
6MWD (m) ^{a,b}	Mean (SD)	412 (91)	295 (85)	520.3 (56.2)
Self reported outcomes				
AM (/100)	Mean (SD)	78.4 (18.5)	64.0 (19.9)	NA
AP (/100)	Mean (SD)	72.2 (14.5)	63.0 (14.2)	NA
FR (/100)	Median (IQR)	76.0 (64.4)	67.6 (59.6)	NA
PR (/100)	Median (IQR)	94.7 (15.1)	95.8 (20.9)	NA
RL (/100)	Mean (SD)	63.4 (24.3)	64.7 (25.4)	NA
SB (/100) ^a	Median (IQR)	93.6 (11.3)	80.13 (34.6)	NA
SO (/100)	Median (IQR)	70.5 (46.0)	85.3 (67.1)	NA
UT (/100)	Median (IQR)	77.9 (18.0)	68.3 (44.7)	NA
WB (/100)	Median (IQR)	86.2 (23.4)	53.8 (61.2)	NA

^aSignificant differences between transtibial and transfemoral amputees, $P \leq 0.05$; ^bSignificant differences between able-bodied and amputee groups. BMI: Body mass index measured with prosthesis on; IQR: Inter-quartile range; nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance; AM: Ambulation; AP: Appearance; FR: Frustration; PR: Perceived response; RL: Residual limb health; SB: Social burden; SO: Sounds; UT: Utility; WB: Well being; NA: Not available; GDI: Gait deviation index.

questions in the PEQ [Larger studies ($n = 135$) by our group have shown that approximately 75% of LLAs experience some form of frustration as measured by the PEQ]. Regression analyses were performed using only participants reporting frustration. The small sample size prohibited separate analysis of the participants who were not frustrated.

Receiver operating characteristic curve

The utility of a regression equation in diagnosing presence of a gait pathology was assessed by constructing receiver operating characteristic (ROC) curves as follows. Participants were classified as either pathological or non-pathological according to their measured GDI and a chosen cut-off, $GDI_{meas,cut}$. In this study, a range of cut-off values for $GDI_{meas,cut}$ were investigated (65-95 in increments of five) because a definitive threshold for amputee gait is not yet available. They were then classified as pathological or non-pathological according to the GDI predicted by the regression equation and a range of cut-off values, $GDI_{pred,cut}$ (55-105, as determined by the GDI_{pred} of each amputee participant). Finally, sensitivity and specificity were calculated for each value of $GDI_{pred,cut}$ and plotted as sensitivity against 1 - specificity. The area under the curve (AUC) was used as an overall measure of performance (AUC = 1 is perfect, AUC = 0.5 is no better than random^[32]). The significance of the two-by-two classification table for a specific value of $GDI_{pred,cut}$

was assessed using Fisher's exact test.

ROC curve analyses were performed using MedCalc for Windows, version 11.4.2.0 (MedCalc Software, Maria-kerke, Belgium). All other analyses, unless otherwise stated, were performed at the 0.05 significance level using Minitab Statistical Software (Version 15).

RESULTS

Participant characteristics

The participant characteristics are summarised in Table 1. The sample was predominantly male (70%) with trauma being the most common reason for amputation (65%). Other reasons for amputation included cancer (10%), infection (10%) and vascular insufficiencies (15%). Two participants with transfemoral amputation used a walking stick during testing; all other participants completed testing unaided. The participant characteristics were similar for the able-bodied group, transtibial amputee group and transfemoral amputee group (Table 1).

Outcome measures

Results for the self-report and performance-based measures are summarised in Table 1. Significant differences were present between the transfemoral and transtibial amputee groups for all performance variables. The transtibial amputee group reported values closer to able-bodied than the transfemoral amputee groups,

Table 2 Correlations with the gait deviation index, Spearman's rank correlation coefficient displayed

Parameter	Correlation coefficient, ρ
Participant characteristics	
Age	-0.13
BMI	-0.27
Age at amputation	-0.16
Time since amputation	0.14
Performance-based outcomes	
nSL _{pro}	0.73 ^b
nSL _{int}	0.83 ^b
nSL _{ave}	0.78 ^b
nSSWS	0.7 ^b
TUGT	-0.60
6MWD	0.74 ^b
Self-report measures	
Ambulation	0.44
Appearance	0.22
Frustration	-0.14
Perceived response	0.02
Residual limb health	-0.22
Social burden	0.37
Sounds	-0.01
Utility	0.33
Well-being	0.20

^b $P \leq 0.001$, indicates significant relationships. BMI: Body mass index measured with prosthesis on; nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance.

but significant differences existed between the amputee groups and able-bodied participants. The transfemoral and transtibial amputees were similar for all scales of the PEQ, except Social Burden, where the transfemoral amputee group reported greater feelings of burden on friends and family as a result of their amputation.

Bivariate analysis

The relationship between the GDI and participant characteristics, performance variables and scales of the PEQ are summarised in Table 2. The GDI demonstrated significant relationships with normalised average step-length, normalised self-selected walking speed (nSSWS) and the 6MWD. Significant correlations were not observed between the GDI, participant characteristics and scales from the PEQ.

Table 3 presents the correlation coefficients for the relationships between the performance-based measures used in this study. The strongest correlation was between nSSWS and 6MWD ($\rho = 0.96$), and all correlations were significant.

Multivariate analysis

The results of multivariate analysis are summarised in Table 4. The 6MWD was the strongest individual predictor of GDI [adjusted R^2 (R^2_{adj}) = 68.6, predictive R^2 (R^2_{pred}) = 60.4], despite intact limb step length producing the greatest adjusted R^2 value (R^2_{adj} = 70.9, R^2_{pred} = 56.8). The forced inclusion of SSWS produced regression equations with the lowest adjusted and

Table 3 Correlations between performance-based measures, Spearman's rank correlation coefficient displayed

	nSL _{pro}	nSL _{int}	nSL _{ave}	nSSWS	TUGT
nSL _{int}	0.87				
nSL _{ave}	0.98	0.95			
nSSWS	0.84	0.91	0.88		
TUGT	-0.70	-0.71	-0.71	-0.82	
6MWD	0.86	0.89	0.89	0.96	-0.83

All correlations significant, $P \leq 0.001$. nSL: Leg-length normalised average step length; nSSWS: Leg-length normalised self selected walking speed; TUGT: Timed-up-and-go test; 6MWD: Six-minute walk distance.

predicted R^2 values. The time taken to stand from a chair with arms (t_{stand} ; derived from the TUGT) and mobility-related questions (particularly AM_C "Over the past four weeks, rate your ability to walk up stair when using your prosthesis", see Table 4) contributed significantly to all regression equations with at least two independent variables.

ROC curve

The equation selected for further analysis predicted GDI using 6MWD, AM_C, t_{stand} and age (R^2_{adj} = 90.2; R^2_{pred} = 86.2; Table 4). It was chosen because of its superior predictive strength and clinical applicability when compared to other regression equations (Table 4). The plot of measured GDI against predicted GDI shown in Figure 1 illustrates the concordance between measured and predicted values for participants in this study.

The resulting ROC curves for a range of measured cut-offs (65-85) are shown in Figure 2. Also in this figure are mean values and 95%CI for AUC for each of the measured cut-offs. The curves and AUC values showed that the diagnostic capability of the regression equation was not sensitive to choice of measured cut-off. Fisher's exact test of the 2×2 classification table gave $P < 0.05$ for all ROC curves.

DISCUSSION

This study has shown that it is possible to predict overall gait deviation, as measured by the GDI, using combinations of simple performance-based and self-report outcome measures in a sample of persons with lower-limb amputation. Of the outcome measures investigated in this study, temporospatial data were the strongest correlates of the GDI (Table 2).

The strongest correlation was observed between the intact limb SL and the GDI (Table 2). This parameter provides insight into the extent of gait asymmetry, which is considered an indication of gait pathology^[33], and explains its strong correlation with the GDI. Asymmetries in prosthetic gait have been attributed to a number of factors, including lack of plantarflexion and decreased range of motion of the prosthetic ankle joint, absence of proprioception and sensory feedback, pain, and prosthetic alignment^[34]. Despite good predictive abilities,

Table 4 Regression analysis; gait deviation index dependent variable

No.	R ² _{adj}	R ² _{pred}	Independent variables			
			1	2	3	4
All variables						
1	70.9	56.8	nSL _{int}			
2	76.1	59.6	nSL _{int}	AM_C		
3	82.6	66.5	nSL _{int}	AM_C	t _{stand}	
4	89.3	81.4	nSL _{int}	AM_C	t _{stand}	6MWD
No step-length parameters						
1	68.6	60.4	6MWD			
2	79.8	72.0	6MWD	AM_C		
3	86.1	82.7	6MWD	AM_C	t _{stand}	
4	90.2	86.2	6MWD	AM_C	t _{stand}	Age
Forced inclusion of walking speed						
1	57.4	46.4	nSSWS			
2	71.1	53.7	nSSWS	AM_C		
3	79.6	65.2	nSSWS	AM_C	t _{stand}	
4	82.1	70.7	nSSWS	AM_C	t _{stand}	UT_D ¹

¹Not significant. Note 1: The table is organized such that the predicted gait deviation index is a function of the independent variables listed. The coefficients of the independent variables have been suppressed until the utility of these equations have been proven for use with individual patients; Note 2: Participants reporting an absence of frustration (*n* = 4) in the four weeks prior to testing were not included in the regression analysis. No.: Number of independent variables; R²_{adj}: Adjusted R²; R²_{pred}: Predictive R²; nSL_{int}: Leg-length normalised intact limb step-length; t_{stand}: Time to stand; AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; 6MWD: Six-minute walk distance; Age: Chronological age; nSSWS: Leg-length normalised self-selected walking speed; UT_D: Over the past four weeks, rate your comfort while standing when using your prosthesis.

these equations are not clinically practical, requiring non-standard technology for the measurement of SL.

Unlike SL, 6MWD and SSWS can be measured with relative ease in clinical contexts. SL and SSWS were mutually exclusive in regression models because of their strong correlation with one another. The 6MWD was more strongly associated with the GDI than walking speed (Table 2) most likely because it is strongly correlated with energy expenditure^[35], and energy expenditure is correlated with gait deviation^[36]. In this study, energy expenditure would have had only minimal impact on SSWS, because the latter was calculated over a distance of only 15 m. The inclusion of 6MWD (Table 4) in the first regression model provides further evidence that energy expenditure is better correlated than walking speed over short distances with gait deviation.

One goal of this study was to develop a set of simple tests that can be used to identify patients whose gait is sufficiently impaired to warrant intervention. The ability of a regression equation to predict measured GDI is encouraging, but an R²_{pred} is a measure of agreement, not a measure of the performance of the equation when used as a diagnostic tool. On the other hand, the ROC curve does provide an overall measure of performance. The areas under the curve (all greater than 0.7; Figure 2), implies that this can be an effective diagnostic tool. Fisher's exact test applied to a range of measured cut-off values confirmed that that the selected regression

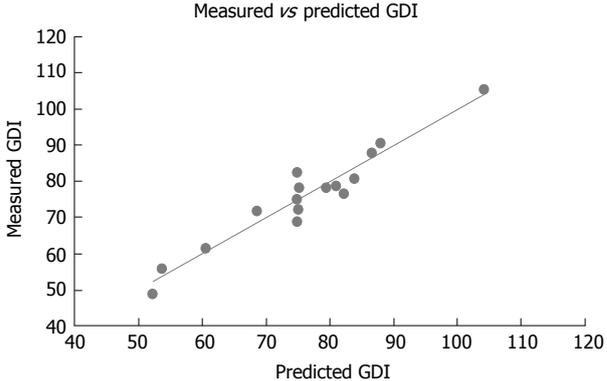


Figure 1 Measured vs predicted gait deviation index for selected equation, constructed using a combination of six-minute walk distance, AM_C, t_{stand} and chronological age (adjusted R² = 90.2; predictive R² = 86.2). AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; t_{stand}: Time taken to stand; GDI: Gait deviation index.

equation was better than chance, *P* < 0.05.

The results from this study indicate that using a battery of outcome measures (excluding 3DGA) in combination provides a better perspective on functional status than using single or only a few measures. This is encouraging, because it implies that low cost and more readily available outcome measures can be highly informative. For example, the effects on function and gait deviation that may arise with changes to componentry would be best assessed using a standardised battery of outcome measures rather than an ad hoc selection of single measures. The statistical analyses demonstrate that characteristics observed across a number of outcome measures may contribute collectively to the quantification of kinematic deviation. In this study, a combination of performance-based and self-report measures provided the best indication of kinematic deviation. The results from this study have shown the ideal outcome measures to assess gait deviation to be: 6MWD, t_{stand}, self-report questions addressing stair climbing and chronological age. Walking speed over longer distances provides a better indication of gait deviation than SSWS over short distances (< 15 m).

Study limitations

The sample size was small and comprised mainly traumatic amputees and experienced prosthetic users. This study did not assess test responsiveness, a necessity for clinical utility. Future work should investigate the responsiveness of the regression models either in response to rehabilitation or componentry modifications, and extend the sample to include more participants with various aetiologies, levels of amputation and prosthetic experience.

The GDI is an overall summary measure of kinematic patterns. It does not, and cannot, substitute for clinical experience and 3DGA. Rather, it provides an efficient method to communicate overall gait pathology. The GDI has demonstrated applicability for use with children with cerebral palsy^[28] and adults with unilateral lower

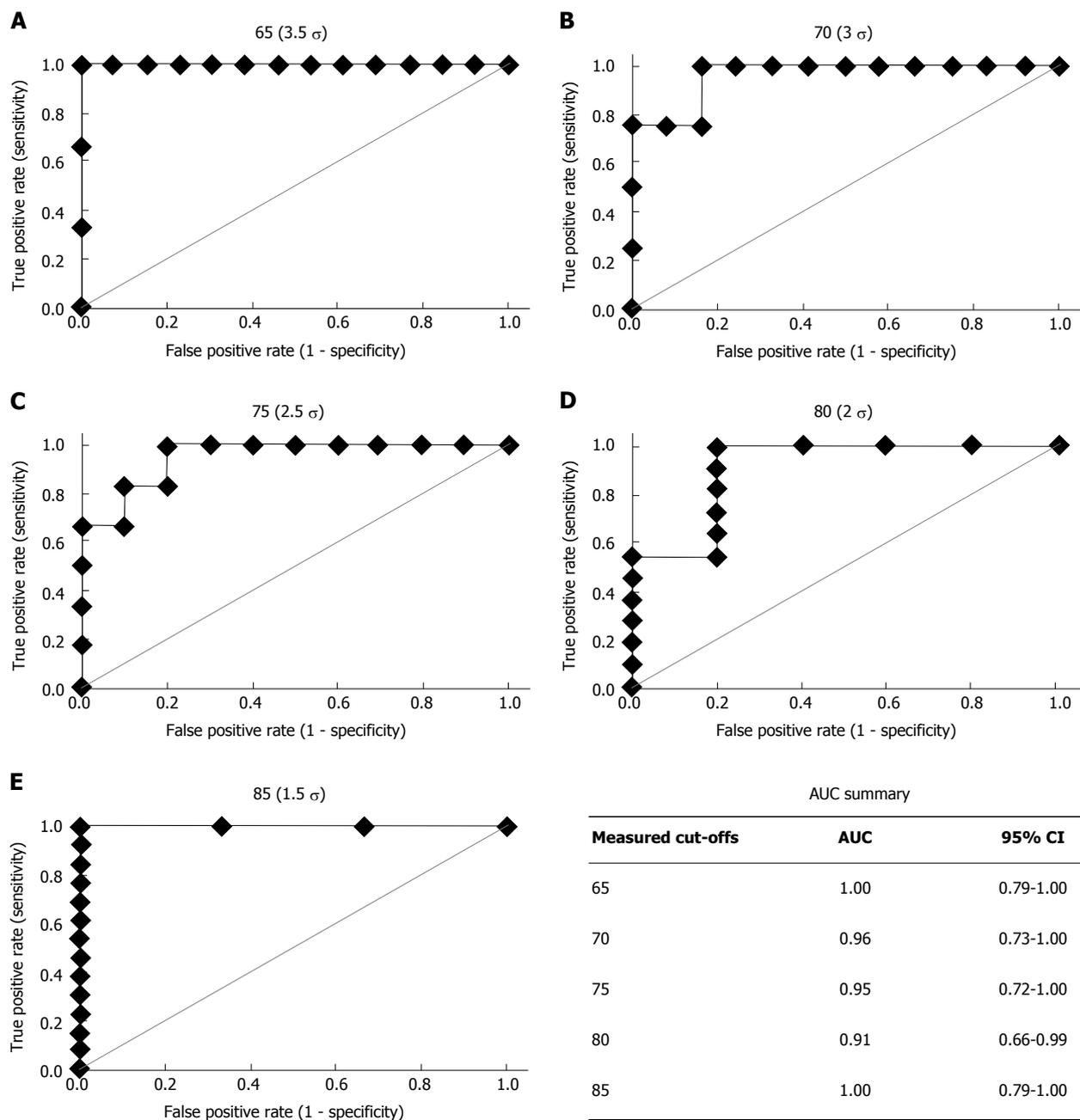


Figure 2 Receiver operating characteristic curves for a range of measured cut-offs [65-85 (A-E), or 3.5-1.5 (A-E) standard deviations (σ) away from the able-bodied mean] for the predictive equation comprised of six-minute walk distance, AM_C, t_{stand} and age. Also included in the bottom right cell are mean values and 95% CIs for AUC for each of the measured cut-offs. AM_C: Over the past four weeks, rate your ability to walk up stairs when using your prosthesis; t_{stand} : Time taken to stand; AUC: Area under the curve.

limb amputation^[37], making it an appropriate outcome measure for use in this study. In addition, kinetic characteristics were excluded, as were data on muscle activation patterns. Both are important measures of gait biomechanics.

Time to stand was derived from the TUGT. In lower functioning individuals there was a clear demarcation between the time to stand and the initiation of walking gait, making the measurement of the time taken to stand relatively straightforward. In contrast, the transition between the standing phased and initiation of walking was sometimes difficult to discern in high functioning

individuals. Some of these participants tucked the intact limb under the chair prior to the start of the test to facilitate forward progression during the standing phase of the TUGT. Where this occurred, the time to stand was recorded as the point at which the trailing leg aligned with the stance limb. Future studies should consider using a designated sit-to-stand test, and contemplate using multiple sit-to-stand assessment such as the five-times sit-to-stand test due to their demonstrated correlation with functional status in older people^[38].

This study offers a practical alternative to quantifying kinematic deviation without conducting complete 3DGA.

Performance-based measures were strong correlates of the GDI, thus rejecting the null hypothesis. It was possible to predict the GDI using a combination of performance-based measures and self-report items related to mobility and prosthetic utility. Accuracy was reasonably high for a range of designated cut-off points for the GDI. Further work is required to determine appropriate GDI cut-off points for each level of amputation.

ACKNOWLEDGMENTS

The authors would like to thank: The Amputee Association of NSW, Inc., and its affiliated branches, for their assistance with recruitment; and Mrs Deborah Vickers for her role in data collection.

COMMENTS

Background

Successful prosthetic fitting is reliant on the appropriate matching of functional ability to prosthetic componentry. But, functional status is not a straightforward concept and its measurement even less so. There are numerous outcome measures currently available, and selection of appropriate measures for the assessment of functional status following lower-limb amputation is complicated. Identifying the smallest subset of appropriate measures required to encapsulate functional status could encourage the systemic and standardised use of outcomes measures throughout the rehabilitation system.

Research frontiers

In comparing the benefits of using self-report vs performance-based measures with older persons, it was shown that neither type of measure is superior, nor are these measures interchangeable. Instead, each assess distinct, although related constructs. Further, self-report and performance-based measures may be complementary. Studies have shown that by complementing performance-based measures with self-report measures it was possible to improve prognostic information in a sample of older person. The challenge remains to determine a suitable combination of self-report and performance-based measures to adequately assess functional status in individuals with lower-limb amputation.

Innovations and breakthroughs

This study has provided a set of simple self-report and performance-based measures to facilitate evaluation of functional status in the physical domain. In this study, functional status was best assessed using a timed walking test, a sit-to-stand assessment and an evaluation of advanced levels of mobility such as stair ambulation. These measures, in combination, enable calculation of overall kinematic deviation in prosthetic users.

Applications

The subset of outcome measures developed in this study that are able to assess kinematic deviation and functional status (in the physical domain) in individuals with lower-limb amputation require no more than a stopwatch and a self-administered questionnaire. All are relatively straightforward to implement in clinical practice. It is hoped that this research will contribute to the development of a standardised set of outcome measures for use within the lower-limb amputation population group, which in turn, will facilitate comparison between rehabilitation facilities and ultimately result in improved outcomes for individuals with lower-limb amputation.

Terminology

GDI: Gait deviation index; a one-dimensional index that summarises kinematic deviation; ROC curve: Receiver operator characteristic curve; illustrates the sensitivity and specificity of a diagnostic test.

Peer-review

This study provides a great foundation for clinicians and researchers looking

for simple, low cost objective and subjective measures to approximate more complex gait analysis. Study design and statistical analysis were appropriate.

REFERENCES

- 1 **Condie E**, Scott H, Treweek S. Lower limb prosthetic outcome measures: A review of the literature 1995 to 2005. *JPO* 2006; **18**: P13-P45 [DOI: 10.1097/00008526-200601001-00004]
- 2 **Ware JE**, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473-483 [PMID: 1593914 DOI: 10.1097/00005650-199206000-00002]
- 3 **Legro MW**, Reiber GD, Smith DG, del Aguila M, Larsen J, Boone D. Prosthesis evaluation questionnaire for persons with lower limb amputations: assessing prosthesis-related quality of life. *Arch Phys Med Rehabil* 1998; **79**: 931-938 [PMID: 9710165 DOI: 10.1016/S003-9993(98)90090-9]
- 4 **Kempen GI**, van Heuvelen MJ, van den Brink RH, Kooijman AC, Klein M, Houx PJ, Ormel J. Factors affecting contrasting results between self-reported and performance-based levels of physical limitation. *Age Ageing* 1996; **25**: 458-464 [PMID: 9003883 DOI: 10.1093/ageing/25.6.458]
- 5 **Carr AJ**, Donovan JL. Why doctors and patients disagree. *Br J Rheumatol* 1998; **37**: 1-4 [PMID: 9487242 DOI: 10.1093/rheumatology/37.1.1a]
- 6 **Smith DG**, Domholdt E, Coleman KL, Del Aguila MA, Boone DA. Ambulatory activity in men with diabetes: relationship between self-reported and real-world performance-based measures. *J Rehabil Res Dev* 2004; **41**: 571-580 [PMID: 15558385]
- 7 **DeLuzio KJ**, Wyss UP, Li J, Costigan PA. A procedure to validate three-dimensional motion assessment systems. *J Biomech* 1993; **26**: 753-759 [PMID: 8514818 DOI: 10.1016/0021-9290(93)90037-F]
- 8 **McGinley JL**, Baker R, Wolfe R, Morris ME. The reliability of three-dimensional kinematic gait measurements: a systematic review. *Gait Posture* 2009; **29**: 360-369 [PMID: 19013070 DOI: 10.1016/j.gaitpost.2008.09.003]
- 9 **Czerniecki JM**, Gitter AJ. Gait analysis in the amputee: Has it helped the amputee or contributed to the development of improved prosthetic components? *Gait Posture* 1996; **4**: 258-268 [DOI: 10.1016/0966-6362(96)01073-9]
- 10 **Cress ME**, Schechtman KB, Mulrow CD, Fiatarone MA, Gerety MB, Buchner DM. Relationship between physical performance and self-perceived physical function. *J Am Geriatr Soc* 1995; **43**: 93-101 [PMID: 7836655 DOI: 10.1111/j.1532-5415.1995.tb06372.x]
- 11 **Reuben DB**, Valle LA, Hays RD, Siu AL. Measuring physical function in community-dwelling older persons: a comparison of self-administered, interviewer-administered, and performance-based measures. *J Am Geriatr Soc* 1995; **43**: 17-23 [PMID: 7806733 DOI: 10.1111/j.1532-5415.1995.tb06236.x]
- 12 **Sherman SE**, Reuben D. Measures of functional status in community-dwelling elders. *J Gen Intern Med* 1998; **13**: 817-823 [PMID: 9844079 DOI: 10.1046/j.1525-1497.1998.00245.x]
- 13 **Stepien JM**, Cavenett S, Taylor L, Crotty M. Activity levels among lower-limb amputees: self-report versus step activity monitor. *Arch Phys Med Rehabil* 2007; **88**: 896-900 [PMID: 17601471 DOI: 10.1016/j.apmr.2007.03.016]
- 14 **Damiano DL**, Abel MF. Relation of gait analysis to gross motor function in cerebral palsy. *Dev Med Child Neurol* 1996; **38**: 389-396 [PMID: 8698147 DOI: 10.1111/j.1469-8749.1996.tb15097.x]
- 15 **Hillman SJ**, Hazlewood ME, Schwartz MH, van der Linden ML, Robb JE. Correlation of the Edinburgh Gait Score with the Gillette Gait Index, the Gillette Functional Assessment Questionnaire, and dimensionless speed. *J Pediatr Orthop* 2007; **27**: 7-11 [PMID: 17195789 DOI: 10.1097/BPO.ob013e31802b7104]
- 16 **Romei M**, Galli M, Fazzi E, Maraucci I, Schwartz M, Uggetti C, Crivellini M. Analysis of the correlation between three methods used in the assessment of children with cerebral palsy. *Funct Neurol* 2007; **22**: 17-21 [PMID: 17509239]
- 17 **Wren TA**, Do KP, Hara R, Dorey FJ, Kay RM, Otsuka NY. Gillette Gait Index as a gait analysis summary measure: comparison with qualitative visual assessments of overall gait. *J Pediatr Orthop*

- 2007; **27**: 765-768 [PMID: 17878782 DOI: 10.1097/BPO/0b013e3181558ade]
- 18 **Novacheck TF**, Stout JL, Tervo R. Reliability and validity of the Gillette Functional Assessment Questionnaire as an outcome measure in children with walking disabilities. *J Pediatr Orthop* 2000; **20**: 75-81 [PMID: 10641694 DOI: 10.1097/01241398-200001000-00017]
- 19 **Tervo RC**, Azuma S, Stout J, Novacheck T. Correlation between physical functioning and gait measures in children with cerebral palsy. *Dev Med Child Neurol* 2002; **44**: 185-190 [PMID: 12005321 DOI: 10.1111/j.1469-8749.2002.tb00784.x]
- 20 **Drouin LM**, Malouin F, Richards CL, Marcoux S. Correlation between the gross motor function measure scores and gait spatio-temporal measures in children with neurological impairments. *Dev Med Child Neurol* 1996; **38**: 1007-1019 [PMID: 8913182 DOI: 10.1111/j.1469-8749.1996.tb15061.x]
- 21 **Archer KR**, Castillo RC, Mackenzie EJ, Bosse MJ. Gait symmetry and walking speed analysis following lower-extremity trauma. *Phys Ther* 2006; **86**: 1630-1640 [PMID: 17138844 DOI: 10.2522/ptj.20060035]
- 22 **Kadaba MP**, Ramakrishnan HK, Wootten ME, Gainey J, Gorton G, Cochran GV. Repeatability of kinematic, kinetic, and electromyographic data in normal adult gait. *J Orthop Res* 1989; **7**: 849-860 [PMID: 2795325 DOI: 10.1007/978-1-4471-5451-8_101]
- 23 **McClelland JA**, Webster KE, Grant C, Feller J. Alternative modelling procedures for pelvic marker occlusion during motion analysis. *Gait Posture* 2010; **31**: 415-419 [PMID: 20176486 DOI: 10.1016/j.gaitpost.2010.01.004]
- 24 **ATS statement: guidelines for the six-minute walk test.** *Am J Respir Crit Care Med* 2002; **166**: 111-117 [PMID: 12091180 DOI: 10.1164/ajrccm.166.1.at1102]
- 25 **Podsiadlo D**, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; **39**: 142-148 [PMID: 1991946 DOI: 10.1111/j.1532.1991.tb01616.x]
- 26 **Lin SJ**, Bose NH. Six-minute walk test in persons with transtibial amputation. *Arch Phys Med Rehabil* 2008; **89**: 2354-2359 [PMID: 18976979 DOI: 10.1016/j.apmr.2008.05.021]
- 27 **Schoppen T**, Boonstra A, Groothoff JW, de Vries J, Göeken LN, Eisma WH. The Timed "up and go" test: reliability and validity in persons with unilateral lower limb amputation. *Arch Phys Med Rehabil* 1999; **80**: 825-828 [PMID: 10414769 DOI: 10.1016/S003-9993(99)90234-4]
- 28 **Schwartz MH**, Rozumalski A. The Gait Deviation Index: a new comprehensive index of gait pathology. *Gait Posture* 2008; **28**: 351-357 [PMID: 18565753 DOI: 10.1016/j.gaitpost.2008.05.001]
- 29 **Zar JH**. Significance Testing of the Spearman Rank Correlation Coefficient. *J Am Stat Assoc* 1972; **67**: 578-580 [DOI: 10.2307/2284441]
- 30 **Steyerberg EW**, Eijkemans MJ, Harrell FE, Habbema JD. Prognostic modelling with logistic regression analysis: a comparison of selection and estimation methods in small data sets. *Stat Med* 2000; **19**: 1059-1079 [PMID: 10790680 DOI: 10.1002/(SICI)1097-0258(20000430)19:8<1059::AID-SIM412>3.0.CO;2.0]
- 31 **Bandura A**. Social foundations of thought and action: a social cognitive theory. Englewood Cliffs, NJ: Prentice Hall, 1986
- 32 **Zweig MH**, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem* 1993; **39**: 561-577 [PMID: 8472349]
- 33 **Sadeghi H**, Allard P, Prince F, Labelle H. Symmetry and limb dominance in able-bodied gait: a review. *Gait Posture* 2000; **12**: 34-45 [PMID: 10996295 DOI: 10.1016/S0966-6362(00)00070-9]
- 34 **Nadollek H**, Brauer S, Isles R. Outcomes after trans-tibial amputation: the relationship between quiet stance ability, strength of hip abductor muscles and gait. *Physiother Res Int* 2002; **7**: 203-214 [PMID: 12528576 DOI: 10.1002/pri.260]
- 35 **Ross RM**, Murthy JN, Wollak ID, Jackson AS. The six minute walk test accurately estimates mean peak oxygen uptake. *BMC Pulm Med* 2010; **10**: 31 [PMID: 20504351 DOI: 10.1186/1471-2466-10-31]
- 36 **Waters RL**, Mulroy S. The energy expenditure of normal and pathologic gait. *Gait Posture* 1999; **9**: 207-231 [PMID: 10575082 DOI: 10.1016/S0966-6362(99)00009-0]
- 37 **Kark L**, Vickers D, McIntosh A, Simmons A. Use of gait summary measures with lower limb amputees. *Gait Posture* 2012; **35**: 238-243 [PMID: 22000790 DOI: 10.1016/j.gaitpost.2011.09.013]
- 38 **Ferrucci L**, Guralnik JM, Studenski S, Fried LP, Cutler GB, Walston JD. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: a consensus report. *J Am Geriatr Soc* 2004; **52**: 625-634 [PMID: 15066083 DOI: 10.1111/j.1532-5415.2004.52174.x]

P- Reviewer: Guerado E, Metzger PD

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Allograft tissue irradiation and failure rate after anterior cruciate ligament reconstruction: A systematic review

Jesse Dashe, Robert L Parisien, Antonio Cusano, Emily J Curry, Asheesh Bedi, Xinning Li

Jesse Dashe, Robert L Parisien, Antonio Cusano, Emily J Curry, Xinning Li, Department of Orthopaedic Surgery, Boston University School of Medicine - Boston Medical Center, Boston, MA 02118, United States

Asheesh Bedi, Department of Orthopaedic Surgery, University of Michigan School of Medicine, Ann Arbor, MI 48105, United States

Author contributions: Dashe J, Parisien RL, Cusano A and Curry EJ were in charge of manuscript write up and assisted with performing the systematic review; Dashe J, Parisien RL, Cusano A, Curry EJ, Bedi A and Li X all reviewed and approved the final version of this manuscript before submission; Bedi A and Li X designed the research study and performed critical review and edits of the manuscript.

Conflict-of-interest statement: All authors report no conflicts of interest regarding this manuscript.

Data sharing statement: All data for this manuscript is available by contacting the corresponding author at xinning.li@gmail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Xinning Li, MD, Department of Orthopaedic Surgery, Boston University School of Medicine - Boston Medical Center, 850 Harrison Avenue - Dowling 2 North, Boston, MA 02118, United States. xinning.li@gmail.com
Telephone: +1-508-8163939
Fax: +1-617-4145226

Received: July 18, 2015
Peer-review started: July 23, 2015
First decision: October 17, 2015
Revised: January 23, 2016
Accepted: March 24, 2016

Article in press: March 25, 2016
Published online: June 18, 2016

Abstract

AIM: To evaluate whether anterior cruciate ligament (ACL) allograft irradiation is effective for sterility without compromising graft integrity and increasing failure rate.

METHODS: A literature search was conducted using PubMed, Cochrane, and Google. The following search terms were used: "Gamma irradiation AND anterior cruciate ligament AND allograft" with a return of 30 items. Filters used included: English language, years 1990-2015. There were 6 hits that were not reviewed, as there were only abstracts available. Another 5 hits were discarded, as they did not pertain to the topic of interest. There were 9 more articles that were excluded: Three studies were performed on animals and 6 studies were meta-analyses. Therefore, a total of 10 articles were applicable to review.

RESULTS: There is a delicate dosing crossover where gamma irradiation is both effective for sterility without catastrophically compromising the structural integrity of the graft. Of note, low dose irradiation is considered less than 2.0 Mrad, moderate dose is between 2.1-2.4 Mrad, and high dose is greater than or equal to 2.5 Mrad. Based upon the results of the literature search, the optimal threshold for sterilization was found to be sterilization at less than 2.2 Mrad of gamma irradiation with the important caveat of being performed at low temperatures. The graft selection process also must include thorough donor screening and testing as well as harvesting the tissue in a sterile fashion. Utilization of higher dose (≥ 2.5 Mrad) of irradiation causes greater allograft tissue laxity that results in greater graft failure rate clinically in patients after ACL reconstruction.

CONCLUSION: Allograft ACL graft gamma irradiated

with less than 2.2 Mrad appears to be a reasonable alternative to autograft for patients above 25 years of age.

Key words: Anterior cruciate ligament reconstruction; Graft choice; Allograft; Gamma irradiation; Anterior cruciate ligament graft failure rate

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The dose of gamma irradiation is directly correlated with increased failure rate of allograft in both *in vitro* and *in vivo* studies. Optimal gamma irradiation dose is less than 2.2 Mrad and should be performed in the setting of a low temperature.

Dashe J, Parisien RL, Cusano A, Curry EJ, Bedi A, Li X. Allograft tissue irradiation and failure rate after anterior cruciate ligament reconstruction: A systematic review. *World J Orthop* 2016; 7(6): 392-400 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/392.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.392>

INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) has been reported to have an incidence of 100000 to 200000 in the United States with about 400000 ACL reconstructions performed worldwide annually^[1,2]. ACL reconstruction is a common procedure in an orthopaedic sports medicine practice and has been shown to have favorable return to play outcomes and preservation of knee function. Both autograft (from the patient) and allograft (cadaver) can be used for the ACL reconstruction procedure^[3]. Advantages of autograft include lower graft failure rate in the young (< 25 years old) and active patient population, lower infection rate, and no risk of disease transmission or immune reaction^[4-7]. Alternatively, advantages of allograft include no donor site morbidity with decreased operative time, earlier return to sports and lower postoperative pain. In the older population, allograft has comparable outcomes compared to autograft reconstruction with a decrease in patient morbidity, surgical time, and smaller incision^[8]. Since using allograft tissue for ACL reconstruction (Figure 1) has proven to be successful in older patients with less physical demands, determining the most favorable processing method of the allograft tissue while minimizing catastrophic failure rates is of paramount importance.

For allograft tissue currently used, it must first undergo a detailed sequence of procedures that include medically and serologically screening donors to rule out viral contamination *via* nucleic acid testing. The Food and Drug Administration and the American Association of Tissue Banks have set industry standards for donor eligibility and tissue preparation. The donor is subjected

to a rigorous physical and medical examination and an array of serological tests to detect antibodies for human immunodeficiency virus 1 and 2, hepatitis C virus, hepatitis B antigen, and syphilis^[9,10]. The rigorous donor selection process serves to eliminate specific contaminants by evaluating the allograft tissue's physical composition, including uniformity in shape and density as well as its biological properties to assess the level of microbial burden and risk for disease transmission^[9,11,12].

After appropriate graft donor selection has occurred, the next step is to sterilize the graft to a sterility assurance level (SAL) of 10^{-6} organism^[9,11,12]. There have been numerous preparations tested to determine the optimal sterilization method including peracetic acid and ethylene oxide, but many of the methods were abandoned after they were found to have detrimental effects on the mechanical properties of the graft and/or cause an inflammatory response in recipients^[13,14]. Other methods of sterilization, such as gamma irradiation, have proven to be more promising. This process uses a source emitting high-frequency electromagnetic radiation to disrupt the DNA (nucleic acids) of living organisms on the tissue to eliminate microbes and inactivating viruses^[15]. The International Atomic Energy Agency has developed a set of standards that govern the proper radiation sterilization of tissue allografts. Their protocol incorporates the principles that were put in place by the International Organization for Standardization to guide the radiation sterilization process of industrially produced health care products^[16].

Some authors cite that anywhere from 0.92-2.5 Mrads is needed to eliminate bacterial bioburden and fungal spores to achieve SAL of 10^{-6} on musculoskeletal allografts^[2,9,12,17,18]. However, the effect of gamma irradiation on viruses is controversial. It has been reported that, in order to inactivate human immunodeficiency virus (HIV) and hepatitis, doses as high as 4.0-5.0 Mrad are required^[17,18].

Unfortunately, gamma irradiation can have destructive effects on allografts by disrupting the polypeptide chain sequence and inducing minor crosslinking without interfering with collagen's normal banding pattern^[19]. There have been reports of gamma irradiation of 3 Mrad causing a reduction on the mechanical properties of the allograft tissue^[20]. Additionally, the temperature at which the gamma irradiation is performed is also important to consider. The mechanical destruction has been reported to be lessened when grafts were irradiated at low temperatures (*i.e.*, on dry ice) when compared to the same process performed at room temperature^[17,21]. However the production of free radicals has also been cited to be a benefit of performing irradiation at higher temperature as the free radicals have anti-microbial effects^[17].

The balance between sterilization of the allograft tissue without compromising the biomechanical properties, strength and functional outcomes is a topic of debate. The purpose of this systematic review article is to further explore the effect of gamma irradiation on



Figure 1 Non-irradiated Achilles allograft tissue. A non-irradiated Achilles tendon allograft used in an anterior cruciate ligament reconstruction procedure.

the catastrophic failure rate and functional outcomes in patients after ACL reconstruction with allograft tissue.

MATERIALS AND METHODS

Systematic review of clinical studies

A literature search was performed using PubMed, Cochrane, and Google with the following search terms with a return of 30 items: "Gamma irradiation AND anterior cruciate ligament AND allograft". Filters used included: English language, years 1990-2015. There were 6 items that were not reviewed, as there were only abstracts available. Another 5 articles were discarded, as they did not pertain to the topic of interest. There were 9 more articles that were excluded: Three studies were performed on animals and 6 studies were meta-analyses. Therefore, a total of 10 clinical articles were applicable to review (Figure 2).

RESULTS

With regards to the effects from gamma irradiation, there are several articles that have extensively studied the effects of irradiation on ACL grafts (Tables 1 and 2). There were four prospective, randomized trials by the same author who attempted to answer this question. The results of these studies all demonstrated that patients who had allografts exposed to > 2.5 Mrad of irradiation had a significantly greater laxity than autograft or non-irradiated allografts; however there were no significant differences in any of these studies on the International Knee Documentation Committee (IKDC) outcome scores or range of motion^[22-25]. Unfortunately, none of these studies report graft temperature during irradiation and therefore should be interpreted with caution. As stated earlier, it is important that the grafts be irradiated at low temperatures to decrease the free radical formation as to not weaken the allograft biomechanical properties^[17,21].

Rappé *et al*^[18] conducted a cohort study comparing non-irradiated Achilles allografts to irradiated Achilles allografts (2.5 Mrad) with the primary outcome of clinical failure (positive Lachman exam, magnetic resonance imaging, and/or side-to-side difference of 5 mm or

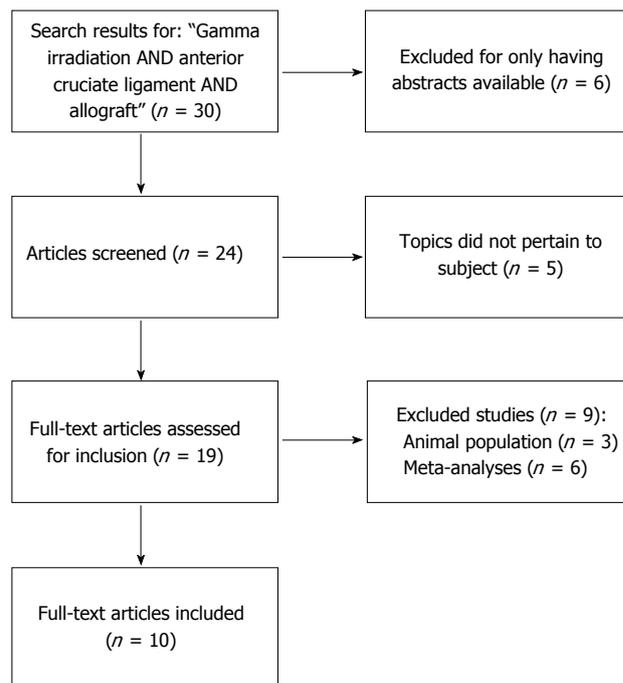


Figure 2 Systematic review of the literature with exclusion and inclusion criteria.

greater on KT-1000 exam). They found that there was a significant difference in clinical failures between the irradiated (33.3%) and non-irradiated groups (2.4%; $P < 0.01$)^[18]. However, there are weaknesses to their study, including a large loss of follow-up in the irradiated group (27%) compared to the non-irradiated group (7%); additionally there was no mention of the temperature at which the irradiation process was performed.

Rihn *et al*^[26] compared the outcomes of bone-patella-tendon-bone (BTB) autograft to BTB allograft that underwent 2.5 Mrad of irradiation. They found no differences in the rate of return to sports or the IKDC scores; however, objectively, the allograft group had significantly more laxity on KT-1000, Lachman exam, and pivot shift clunk. However, similar to Rappé *et al*^[18], this study made no mention of temperature of the graft preparation and had significant differences in the mean age of the two study groups with the allograft group having an older mean age.

The increase in laxity and failure rates was also noted in the studies by Sun *et al*^[22-25] with 34% failure seen in the irradiated allograft group (2.5 Mrad), 6.4% in the autograft group and 8.8% in the nonirradiated allograft group. Sun *et al*^[23] compared hamstring autograft to irradiated allograft with over 2.5 years of follow-up and reported the rate of laxity was 32% higher in the irradiated vs autograft group (8.3%). In addition, anterior and rotational stability also decreased significantly in the irradiated allograft group; however, the IKDC functional scores were very similar between the two groups. In a subsequent follow-up randomized controlled trial comparing irradiated to nonirradiated hamstring allograft for ACL reconstruction, Sun *et al*^[24] found that allograft irradiation is responsible for increased anterior and

Table 1 *In vivo* studies of non-irradiated and irradiated allograft tissue for anterior cruciate ligament reconstruction

Ref.	Year	Type of study	Graft type	Irradiation dose	No. of patients (at final follow-up/enrolled)	Male	Female	Average age (yr)	Follow-up length	Findings	Weaknesses
Rihn <i>et al</i> ^[26]	2006	Retrospective	BPTB - allograft	2.5 Mrad	39	27	12	44 ± 8.4	4.2 yr	Significant difference between irradiated allograft and allograft with laxity, Lachman, and pivot shift clunk	Age difference in populations
Rappé <i>et al</i> ^[18]	2007	Cohort	BPTB - autograft Achilles - allograft	None 2.0-2.5 Mrad	63 33/45	43 N/A	20 N/A	25.3 ± 9.3 26 (range 14-59)	4.6 yr 6 mo	No significant difference on range of motion, effusion, IKDC, KT-1000 when adjusted for age, IKDC physical exam rating, and return to sport Significantly more clinical failures in irradiated allograft vs non-irradiated allograft groups with failures occurring about 9 mo earlier in irradiated group (failure of graft = 5 mm or greater on KT-1000 compared to contralateral side, positive Lachman, or magnetic resonance imaging)	No mention of temperature when irradiation performed Large loss of follow-up in irradiated group No mention of temperature when irradiation performed
Sun <i>et al</i> ^[22]	2009	Prospective, randomized	BPTB - allograft	2.5 Mrad	32/33	24	8	30.1 ± 6.1	31 mo (2% lost to follow-up)	Significant difference between irradiated allograft and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade II or III, anterior drawer test grade II or III, and Lachman test grade II or III No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	No mention of temperature when irradiation performed No mention of temperature when irradiation performed
Sun <i>et al</i> ^[23]	2009	Prospective, randomized	BPTB - allograft BPTB - allograft	2.5 Mrad None	32 34	24 22	8 12	30.1 ± 6.1 31.8 ± 6.9	31 mo (1% lost to follow-up - treatment group not mentioned)	Significant difference between irradiated allograft, non-irradiated allograft, and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade II or III, anterior drawer test grade II or III, and Lachman test grade II or III No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	No mention of temperature when irradiation performed
Sun <i>et al</i> ^[24]	2011	Prospective, randomized	Hamstring - allograft Hamstring - autograft	2.5 Mrad None	31/37 36/38	24 28	7 8	30.3 ± 7.9 30.9 ± 8.7	42.2 mo (11% lost to follow-up)	Significant difference between irradiated allograft and autograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade II or III, anterior drawer test grade II or III, and Lachman test grade II or III No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	No mention of temperature when irradiation performed

Sun <i>et al.</i> ^[25]	2012	Prospective, randomized	Hamstring - allograft	2.5 Mrad	31/38	24	7	30.3 ± 7.9	42.5 mo (9.1% lost to follow-up)	Significant difference between irradiated allograft and non-irradiated allograft with greater laxity on KT-2000, side to side difference on KT-2000, pivot shift grade II or III, anterior drawer test grade II or III, and Lachman test grade II or III	No mention of temperature when irradiation performed
			Hamstring - allograft	None	38/39	31	7	31.7 ± 7.8		No significant difference on overall IKDC, range of motion, Harner's vertical jump test, Daniel's one-leg hip test, subjective IKDC, Cincinnati knee score, Lysholm score, and Tegner score	

IKDC: International Knee Documentation Committee; BPTB: Bone patella tendon bone.

rotational instability. Furthermore, the knees that had an ACL reconstruction done with the irradiated graft has significantly more osteoarthritis compared to the nonirradiated group.

In biomechanical testing, Roche *et al.*^[27] evaluated the effect on gamma irradiation (1.55 Mrad on dry ice or low temperature) with BTB and fascia lata allografts. The authors found no significant difference between the irradiated group and the non-irradiated groups when testing the grafts' tensile strength. Balsly *et al.*^[9] also reported on the effect of low (1.8-2.2 Mrad) vs high dose (2.4-2.8 Mrad) irradiation on the biomechanical properties of allograft tissue (BTB, anterior tibialis, semitendinosus, and fascia lata allografts). All irradiation processing was performed at low temperatures. For the low dose irradiation groups for all types of allografts mentioned, there were no significant difference found between the control groups and the low dose irradiation groups when the tensile strength or modulus of elasticity of the grafts was tested. For the moderate irradiation group, there was either a significant difference or a trend towards having a significant difference when compared to the controls in these same measures.

Fideler *et al.*^[28] also demonstrated that the initial biomechanical strength of allografts was reduced 15% when compared to controls after 2 Mrad of irradiation. He also showed a dose dependent effect on the integrity of the allograft tissue with increasing gamma irradiation at 3 and 4 Mrads. Curran *et al.*^[29] reported the average load to failure of irradiated patellar tendon grafts vs nonirradiated grafts was 1965 ± 512 N vs 2457 ± 647 N, respectively. Furthermore, with cyclic loading, the irradiated grafts elongated 27% more than the nonirradiated grafts ($P < 0.05$).

DISCUSSION

The choice of graft for ACL reconstruction is contingent upon many factors including the age, baseline level of activity, and planned level of future activities^[2,3,30]. Much of the debate about whether to use allograft or autograft for ACL reconstruction is related to the morbidity and complications related to each option. Autograft procedures have the disadvantage of increased surgical time due to graft harvesting, which can translate into higher procedural costs (*i.e.*, operating room time). Additional autograft harvesting risks include quadriceps or hamstring weakness from quadriceps/hamstring grafts and anterior knee pain from the BTB procedures. The benefits of using autograft include minimal risk of infection/disease transmission from donated tissue, no possibility of immune reaction to the graft (other than increased OR time), and an overall decreased rerupture rate in younger patients under the age of 25 years^[2,3,11,22,31].

Reconstruction using allograft has its own unique risks. There are risks of immunogenic reaction, bacterial infection, and disease transmission from the graft donor. However, it has been reported that HIV or hepatitis transmission is 1 in 1.6 million^[2,9,17,18,21,26,31,32]. The possibility of an immune reaction stems from the body's response to foreign tissues via interactions to human leukocyte antigens (HLAs) on donor cells. Fortunately, recent studies have found that an immune response to allograft tissue has not been a common issue, since the allograft tissue processing (*i.e.*, the freezing process) essentially eliminates active HLA markers^[2,31]. Another cited disadvantage of allograft use is increased laxity over time, which can result in knee laxity and failure to return to previous level of activities despite an "intact" graft^[31]. Some of the cited advantages of using allograft include smaller incisions, reduced postoperative pain/less donor site morbidity (since no graft harvesting is required), larger graft availability, earlier postoperative knee range of

Table 2 *In vitro* studies of non-irradiated and irradiated allograft tissue for anterior cruciate ligament reconstruction

Ref.	Year	Type of study	Graft type	Irradiation dose	Temperautre when irradiated	No. of samples	Age (yr)	Findings							
Balsly <i>et al</i> ^[9]	2008	Laboratory	BPTB - low dose	1.83-2.18 Mrad	- 20 °C to -50 °C	9	18-55	There was a significant difference for: (1) BPTB - tensile strength in the moderate dose irradiation <i>vs</i> control groups (2) Fascia lata - modulus of elasticity in the moderate dose irradiation <i>vs</i> control groups No significant difference between the tensile strength and modulus of elasticity for all other groups for low dose irradiation <i>vs</i> control and moderate dose irradiation <i>vs</i> control (other than stated above)							
			BPTB - moderate dose	2.4-2.85 Mrad		9									
			BPTB - control	None	N/A	9 controls for low dose 9 controls moderate dose									
			Anterior Tibialis - low dose	1.83-2.18 Mrad	- 20 °C to -50 °C	10	23-64								
			Anterior Tibialis - moderate dose	2.4-2.85 Mrad		10									
			Anterior Tibialis - control	None	N/A	10 controls for low dose 10 controls for moderate dose									
			Semitendinosus - low dose	1.83-2.18 Mrad	- 20 °C to -50 °C	8	16-54								
			Semitendinosus - moderate dose	2.4-2.85 Mrad		10									
			Semitendinosus - control	None	N/A	10 controls for low dose 10 controls for moderate dose									
			Fascia Lata - low dose	1.83-2.18 Mrad	- 20 °C to -50 °C	10	19-48								
			Fascia Lata - moderate dose	2.4-2.85 Mrad		10									
			Fascia Lata - control	None	N/A	10 controls for low dose 10 controls for moderate dose									
			Greaves <i>et al</i> ^[17]	2008	Laboratory	Tibialis - single strand irradiated (age < 45)	1.46-1.8 Mrad		Dry ice temperatures	10 irradiated	< 45	No significant difference in failure loads for irradiated <i>vs</i> non-irradiated for each of the three age groups (midsubstance failure = any rupture within graft substance, grip failure = slip from 1 of tendon grips exposing serrated portion of tendon)			
						Tibialis - single strand non-irradiated (age < 45)				10 non-irradiated					
Tibialis - double strand irradiated (age < 45)	10 irradiated														
Tibialis - double strand non-irradiated (age < 45)	10 non-irradiated														
Tibialis - single strand irradiated (age 46-55)	13 irradiated	46-55													
Tibialis - single strand non-irradiated (age 46-55)	13 non-irradiated														
Tibialis - double strand irradiated (age 46-55)	10 irradiated														
Tibialis - double strand non-irradiated (age 46-55)	10 non-irradiated														
Tibialis - single strand irradiated (age 56-65)	10 irradiated	56-65													
Tibialis - single strand non-irradiated (age 56-65)	10 non-irradiated														
Tibialis - double strand irradiated (age 56-65)	10 irradiated														
Tibialis - double strand non-irradiated (age 56-65)	10 non-irradiated														
Baldini <i>et al</i> ^[34]	2012	Laboratory				Tibialis		2.0-2.8 Mrad		Not reported			15	41.8	There were no significant difference in stiffness, failure to load, and failure stress between the irradiated <i>vs</i> non-irradiated groups
								None					12		

Yanke <i>et al</i> ^[35]	2013	Laboratory	BPTB	1.0-1.2 Mrad None	Not reported	10 10	52 ± 11	There was a significant difference in stiffness between the irradiated <i>vs</i> non-irradiated groups but none found in strain and elongation
------------------------------------	------	------------	------	-------------------------	--------------	--------------	---------	--

BPTB: Bone patella tendon bone.

motion, and decreased surgical time^[2,11].

A discussion with patients about graft integrity is important when allograft is being used for ACL reconstruction. There have been reports about having decreased allograft strength after gamma irradiation, which clinically manifests as laxity and/or catastrophic graft failure. This has been a controversial topic with conflicting studies attributed to the lack of details about how grafts were processed including the irradiation dose and the graft temperature during irradiation^[9,17,18,21,26,32]. Our review of the literature found that utilizing the higher dose (≥ 2.5 Mrad) of irradiation causes greater allograft tissue laxity and subsequently increased graft failure rate. However, in the subset of patients that did not have catastrophic failures from the irradiated graft, overall functional outcome as measured by the IKDC scores were similar to the nonirradiated allograft or autograft groups. Ghodadra *et al*^[33], compared BTB autograft and Patellar tendon allograft (nonirradiated and low dose irradiation - 1.0 to 1.3 Mrad) using a retrospective cohort and found no differences in postoperative laxity (KT-1000) or failure rates at 6 wk and 1 year. Additionally, the authors found no difference in the laxity between the patellar tendon groups that had the low dose irradiation *vs* no irradiation.

The choice to use an irradiated graft is contingent upon many factors. The important details to know when choosing an irradiated graft are: How the graft was prepared, the dose range of irradiation used, and the temperature of the graft when the irradiation was performed. The results from our systematic review suggest that grafts that are irradiated at low temperatures with 1.8 to 2.2 Mrad of irradiation do not appear to have deleterious effects on the allograft tissue tensile strength or elasticity modulus. However, moderate to high doses of gamma radiation (≥ 2.5 Mrad) will have a major impact on the allograft tissue biomechanical properties which may result in increased laxity that may compromise clinical outcomes and increase rates of functional failure. These above studies suggest that grafts irradiated at low temperatures with less than 2.2 Mrad of irradiation are an acceptable choice to optimize the benefits of sterility and without affecting rate of functional or catastrophic structural failure.

There have been large advancements in allograft tissue processing for ACL reconstruction over the past several decades. There are many advantages of using allograft for ACL reconstruction in the older and less active population when compared to autograft with similar functional outcomes. The concerns of infection with allografts have been mitigated by the changes in the tissue bank facility practices with improved donor tissue screening and use of gamma irradiation. Irradiation has

proven to be successful at reducing the bioburden found on allografts (and possibly viral contamination) and appears to not have an effect on the rate of functional failure if it is performed with low dose irradiation (< 2.2 Mrad) at low temperatures. Grafts prepared with higher dose irradiation (≥ 2.5 Mrad) may be weakened and the additional irradiation may compromise the graft's biomechanical properties and clinical outcomes resulting in unacceptable failure rates.

COMMENTS

Background

Anterior cruciate ligament (ACL) reconstruction is a common procedure in the orthopaedic sports medicine practice. The surgery involves using tissue either from the patient (autograft) and/or from cadaver (allograft). It has been shown that the failure rates when comparing allograft to autograft tissue decreases with increased age.

Research frontiers

One of the main concerns with the use of allograft is the balance between the process of graft sterilization and its potential impact on graft integrity. It has been suggested that there is an association between increased gamma irradiation dosage and an adverse impact on the biomechanical properties of the allograft tissue, although controversy remains with regards to dosing thresholds that will compromise the strength of the allograft tissue.

Innovations and breakthroughs

There has been a trend toward increased allograft use in older and lower demand patients in recent years in an effort to decrease the morbidity associated with autograft harvest. With increased allograft use, appropriate graft irradiation exposure has been investigated. Four prospective, randomized trials demonstrated that patients who had allografts exposed to greater than or equal to 2.5 Mrad of irradiation had a significantly greater laxity and clinical failure rates than autograft or non-irradiated (< 2.2 Mrad) allografts (all different studies), but temperature at time of irradiation was not recorded. It is also important that the grafts be irradiated at low temperatures to decrease the free radical formation as to not weaken the allograft.

Applications

The authors used a systematic review of the currently available literature to determine that there is a delicate dosing crossover where gamma irradiation is both effective for sterility without catastrophically compromising the graft structural integrity.

Terminology

Gamma irradiation is a means of allograft sterilization, which uses a source emitting high-frequency electromagnetic radiation to disrupt the DNA (nucleic acids) of living organisms on the tissue.

Peer-review

This is a useful systematic review on the use of allograft for ACL reconstruction particularly focusing on the effect of the sterilization process on its biomechanical properties and clinical outcomes. The authors introduce the reader to the ACL reconstruction graft options, sterilization process and associated clinical and laboratory results. This review gives readers the opportunity to implement to their

practice a better use and understanding of gamma irradiation of allograft tissues for ACL reconstruction.

REFERENCES

- 1 **Rayan F**, Nanjayan SK, Quah C, Ramoutar D, Konan S, Haddad FS. Review of evolution of tunnel position in anterior cruciate ligament reconstruction. *World J Orthop* 2015; **6**: 252-262 [PMID: 25793165 DOI: 10.5312/wjo.v6.i2.252]
- 2 **Klimkiewicz JJ**, Brian J, Samsell BJ, Riff A, DeBarardino TM, Moore MA. Comparison of human tendon allografts and autografts used in knee reconstruction. *Current Orthopaedic Practice* 2011; **22**: 494-502 [DOI: 10.1097/BCO.0b013e318236c466]
- 3 **Kaeding CC**, Aros B, Pedroza A, Pifel E, Amendola A, Andrish JT, Dunn WR, Marx RG, McCarty EC, Parker RD, Wright RW, Spindler KP. Allograft Versus Autograft Anterior Cruciate Ligament Reconstruction: Predictors of Failure From a MOON Prospective Longitudinal Cohort. *Sports Health* 2011; **3**: 73-81 [PMID: 23015994 DOI: 10.1177/1941738110386185]
- 4 **Arnoczky SP**, Warren RF, Ashlock MA. Replacement of the anterior cruciate ligament using a patellar tendon allograft. An experimental study. *J Bone Joint Surg Am* 1986; **68**: 376-385 [PMID: 3949832]
- 5 **Prodromos C**, Joyce B, Shi K. A meta-analysis of stability of autografts compared to allografts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 851-856 [PMID: 17437083 DOI: 10.1007/s00167-007-0328-6]
- 6 **Crawford C**, Kainer M, Jernigan D, Banerjee S, Friedman C, Ahmed F, Archibald LK. Investigation of postoperative allograft-associated infections in patients who underwent musculoskeletal allograft implantation. *Clin Infect Dis* 2005; **41**: 195-200 [PMID: 15983915 DOI: 10.1086/430911]
- 7 **Malinin TI**, Levitt RL, Bashore C, Temple HT, Mnaymneh W. A study of retrieved allografts used to replace anterior cruciate ligaments. *Arthroscopy* 2002; **18**: 163-170 [PMID: 11830810 DOI: 10.1053/jars.2002.30485]
- 8 **Barrett G**, Stokes D, White M. Anterior cruciate ligament reconstruction in patients older than 40 years: allograft versus autograft patellar tendon. *Am J Sports Med* 2005; **33**: 1505-1512 [PMID: 16009990 DOI: 10.1177/0363546504274202]
- 9 **Balsly CR**, Cotter AT, Williams LA, Gaskins BD, Moore MA, Wolfenbarger L. Effect of low dose and moderate dose gamma irradiation on the mechanical properties of bone and soft tissue allografts. *Cell Tissue Bank* 2008; **9**: 289-298 [PMID: 18431690 DOI: 10.1007/s10561-008-9069-0]
- 10 Title 21 - Food and Drugs: Part 1271 Human Cells, Tissues, and Cellular and Tissue-Derived Products. 2014 April 1, 2014. Available from: URL: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=1271>
- 11 **McKee J**. Autograft or Allograft for ACL Reconstruction? 2012. [Accessed 26 October 2015]. Available from: URL: <http://www.aaos.org/news/aaosnow/apr12/cover1.asp>
- 12 **Baker TF**, Ronholdt CJ, Bogdansky S. Validating a low dose gamma irradiation process for sterilizing allografts using ISO 11137 method 2B. *Cell Tissue Bank* 2005; **6**: 271-275 [PMID: 16308766 DOI: 10.1007/s10561-005-7364-6]
- 13 **Scheffler SU**, Scherler J, Pruss A, von Versen R, Weiler A. Biomechanical comparison of human bone-patellar tendon-bone grafts after sterilization with peracetic acid ethanol. *Cell Tissue Bank* 2005; **6**: 109-115 [PMID: 15909098 DOI: 10.1007/s10561-004-6403-z]
- 14 **Scheffler SU**, Gonnermann J, Kamp J, Przybilla D, Pruss A. Remodeling of ACL allografts is inhibited by peracetic acid sterilization. *Clin Orthop Relat Res* 2008; **466**: 1810-1818 [PMID: 18491201 DOI: 10.1007/s11999-008-0288-2]
- 15 **Mikhael MM**, Huddleston PM, Zobitz ME, Chen Q, Zhao KD, An KN. Mechanical strength of bone allografts subjected to chemical sterilization and other terminal processing methods. *J Biomech* 2008; **41**: 2816-2820 [PMID: 18760413 DOI: 10.1016/j.jbiomech.2008.07.012]
- 16 Radiation sterilization of tissue allografts-requirements for validation and routine control A code of practice. IAEA 2007: 55. Available from: URL: http://www-pub.iaea.org/MTCD/publications/PDF/Pub1307_web.pdf
- 17 **Greaves LL**, Hecker AT, Brown CH. The effect of donor age and low-dose gamma irradiation on the initial biomechanical properties of human tibialis tendon allografts. *Am J Sports Med* 2008; **36**: 1358-1366 [PMID: 18400948 DOI: 10.1177/0363546508314394]
- 18 **Rappé M**, Horodyski M, Meister K, Indelicato PA. Nonirradiated versus irradiated Achilles allograft: in vivo failure comparison. *Am J Sports Med* 2007; **35**: 1653-1658 [PMID: 17517908 DOI: 10.1177/0363546507302926]
- 19 **De Deyne P**, Haut RC. Some effects of gamma irradiation on patellar tendon allografts. *Connect Tissue Res* 1991; **27**: 51-62 [PMID: 1773614 DOI: 10.3109/03008209109006994]
- 20 **Schwartz HE**, Matava MJ, Proch FS, Butler CA, Ratcliffe A, Levy M, Butler DL. The effect of gamma irradiation on anterior cruciate ligament allograft biomechanical and biochemical properties in the caprine model at time zero and at 6 months after surgery. *Am J Sports Med* 2006; **34**: 1747-1755 [PMID: 16735581 DOI: 10.1177/0363546506288851]
- 21 **Samsell BJ**, Moore MA. Use of controlled low dose gamma irradiation to sterilize allograft tendons for ACL reconstruction: biomechanical and clinical perspective. *Cell Tissue Bank* 2012; **13**: 217-223 [PMID: 21431365 DOI: 10.1007/s10561-011-9251-7]
- 22 **Sun K**, Tian S, Zhang J, Xia C, Zhang C, Yu T. Anterior cruciate ligament reconstruction with BPTB autograft, irradiated versus non-irradiated allograft: a prospective randomized clinical study. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 464-474 [PMID: 19139845 DOI: 10.1007/s00167-008-0714-8]
- 23 **Sun K**, Tian SQ, Zhang JH, Xia CS, Zhang CL, Yu TB. ACL reconstruction with BPTB autograft and irradiated fresh frozen allograft. *J Zhejiang Univ Sci B* 2009; **10**: 306-316 [PMID: 19353750 DOI: 10.1631/jzus.B0820335]
- 24 **Sun K**, Zhang J, Wang Y, Xia C, Zhang C, Yu T, Tian S. Arthroscopic anterior cruciate ligament reconstruction with at least 2.5 years' follow-up comparing hamstring tendon autograft and irradiated allograft. *Arthroscopy* 2011; **27**: 1195-1202 [PMID: 21782375 DOI: 10.1016/j.arthro.2011.03.083]
- 25 **Sun K**, Zhang J, Wang Y, Zhang C, Xia C, Yu T, Tian S. A prospective randomized comparison of irradiated and non-irradiated hamstring tendon allograft for ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 187-194 [PMID: 21290113 DOI: 10.1007/s00167-010-1393-9]
- 26 **Rihn JA**, Irrgang JJ, Chhabra A, Fu FH, Harner CD. Does irradiation affect the clinical outcome of patellar tendon allograft ACL reconstruction? *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 885-896 [PMID: 16502300 DOI: 10.1007/s00167-006-0036-7]
- 27 **Roche C**, Gaskins B, Kuhn C, Moore M. The effects of gamma irradiation on the biomechanical properties of soft tissue allografts. 2005. Available from: URL: <http://www.aatb.org/files/2005Abstract37.pdf>
- 28 **Fideler BM**, Vangness CT, Lu B, Orlando C, Moore T. Gamma irradiation: effects on biomechanical properties of human bone-patellar tendon-bone allografts. *Am J Sports Med* 1995; **23**: 643-646 [PMID: 8526284]
- 29 **Curran AR**, Adams DJ, Gill JL, Steiner ME, Scheller AD. The biomechanical effects of low-dose irradiation on bone-patellar tendon-bone allografts. *Am J Sports Med* 2004; **32**: 1131-1135 [PMID: 15262633 DOI: 10.1177/0363546503260060]
- 30 **Gifstad T**, Foss OA, Engebretsen L, Lind M, Forssblad M, Albrektsen G, Drogset JO. Lower risk of revision with patellar tendon autografts compared with hamstring autografts: a registry study based on 45,998 primary ACL reconstructions in Scandinavia. *Am J Sports Med* 2014; **42**: 2319-2328 [PMID: 25201444 DOI: 10.1177/0363546514548164]
- 31 **Singhal MC**, Gardiner JR, Johnson DL. Failure of primary anterior cruciate ligament surgery using anterior tibialis allograft. *Arthroscopy* 2007; **23**: 469-475 [PMID: 17478276 DOI: 10.1016/j.arthro.2006.12.010]
- 32 **Moore MA**. Inactivation of enveloped and non-enveloped

- viruses on seeded human tissues by gamma irradiation. *Cell Tissue Bank* 2012; **13**: 401-407 [PMID: 21809182 DOI: 10.1007/s10561-011-9266-0]
- 33 **Ghodadra NS**, Mall NA, Grumet R, Sherman SL, Kirk S, Provencher MT, Bach BR. Interval arthrometric comparison of anterior cruciate ligament reconstruction using bone-patellar tendon-bone autograft versus allograft: do grafts attenuate within the first year postoperatively? *Am J Sports Med* 2012; **40**: 1347-1354 [PMID: 22451585 DOI: 10.1177/0363546512440685]
- 34 **Baldini T**, Caperton K, Hamkins M, McCarty E. Effect of a novel sterilization method on biomechanical properties of soft tissue allografts. *Knee Surg Sports Traumatol Arthrosc* 2014; Epub ahead of print [PMID: 25100489]
- 35 **Yanke AB**, Bell R, Lee AS, Shewman E, Wang VM, Bach BR. Central-third bone-patellar tendon-bone allografts demonstrate superior biomechanical failure characteristics compared with hemipatellar tendon grafts. *Am J Sports Med* 2013; **41**: 2521-2526 [PMID: 24007760 DOI: 10.1177/0363546513501780]

P- Reviewer: Drampalos E, Metzger PD
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Posterolateral dislocation of the knee: Recognizing an uncommon entity

Colin YL Woon, Mark R Hutchinson

Colin YL Woon, Mark R Hutchinson, Department of Orthopaedic Surgery, University of Illinois at Chicago, Chicago, IL 60612, United States

Author contributions: Woon CYL designed the report and wrote the paper; Hutchinson MR co-wrote and reviewed the paper for critical content.

Institutional review board statement: None.

Informed consent statement: The involved subject provided written informed consent for the study.

Conflict-of-interest statement: The authors declare no conflicts of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Colin YL Woon, MD, Department of Orthopaedic Surgery, University of Illinois at Chicago, 835 S. Wolcott Avenue, M/C 844, Chicago, IL 60612, United States. wolv23@gmail.com
Telephone: +1-312-9969858
Fax: +1-312-9969025

Received: February 3, 2016

Peer-review started: February 3, 2016

First decision: March 21, 2016

Revised: March 23, 2016

Accepted: April 7, 2016

Article in press: April 11, 2016

Published online: June 18, 2016

Abstract

Posterolateral dislocations of the knee are rare injuries. Early recognition and emergent open reduction is crucial. A 48-year-old Caucasian male presented with right knee pain and limb swelling 3 d after sustaining a twisting injury in the bathroom. Examination revealed the pathognomonic anteromedial "pucker" sign. Ankle-brachial indices were greater than 1.0 and symmetrical. Radiographs showed a posterolateral dislocation of the right knee. He underwent emergency open reduction without an attempt at closed reduction. Attempts at closed reduction of posterolateral dislocations of the knee are usually impossible because of incarceration of medial soft tissue in the intercondylar notch and may only to delay surgical management and increase the risk of skin necrosis. Magnetic resonance imaging is not crucial in the preoperative period and can lead to delays of up to 24 h. Instead, open reduction should be performed once vascular compromise is excluded.

Key words: Knee dislocation; Irreducible dislocation; Medial patellofemoral ligament; Vastus medialis; Medial collateral ligament

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Posterolateral knee dislocations are uncommon injuries that are often missed or misdiagnosed. We believe that attempts at closed reduction and preoperative magnetic resonance imaging are unnecessary delays to open reduction. We advocate emergent open reduction once vascular integrity is confirmed on ankle-brachial index testing.

Woon CYL, Hutchinson MR. Posterolateral dislocation of

the knee: Recognizing an uncommon entity. *World J Orthop* 2016; 7(6): 401-405 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i6/401.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i6.401>

INTRODUCTION

Posterolateral dislocation of the knee is an uncommon injury. Closed reduction is not possible because of incarceration of medial soft tissue^[1,2] and should not be attempted. Open reduction is indicated once this condition is diagnosed and vascular integrity is confirmed. We present a case with posterolateral knee dislocation that presented 3 d after the original injury and discuss the successful management of this injury.

We have obtained the patient's written informed consent for print and electronic publication of the report. There are no conflicts of interest.

CASE REPORT

A 48-year-old male slipped and fell in the bathroom, striking his knee on the bathtub and sustaining a twisting injury to his right knee. He was only able to bear minimal weight on the extremity, and lay on his bed for 3 d prior to presentation. His roommates finally called for an ambulance because of unrelenting pain and increasing swelling of the entire lower extremity. His history was otherwise unremarkable except for smoking (a few cigarettes a day) and alcohol use (1 can of beer every few days).

On presentation in the emergency room, the limb was grossly swollen from the mid-thigh to the ankle, with blistering over the distal anteromedial thigh. The knee was held in slight flexion. There was ecchymotic discoloration and transverse "puckering" over the distal anteromedial thigh, and a smooth, bony prominence was palpable subcutaneously proximal to the "pucker" (Figure 1). There was diffuse tenderness around the knee. Leg swelling was soft and not suggestive of compartment syndrome. Dorsalis pedis and posterior tibial pulses were strong and the foot was warm and pink. The ankle-brachial index (ABI) exceeded 1.0 for both lower extremities. Toe plantar- and dorsiflexion strength was Medical Research Council Grade 5 and sensation was preserved. Radiographs revealed a posterolateral dislocation of the knee (Figure 2). He was taken to the operating room emergently that evening.

Under general anesthesia, the knee was inspected and brought through its range of motion (Figure 3). Under tourniquet control, and incision was made over the anteromedial leg and thigh, directly over the "pucker". There was a large rent in the medial soft tissue, and the medial femoral condyle was found lying in the subcutaneous plane. The medial patellar retinaculum, capsule, medial patellofemoral ligament (MPFL), vastus medialis, meniscotibial and meniscofemoral ligaments were found incarcerated within the intercondylar notch of the femur.

These tissues were freed and reduced back to their original subcutaneous position, allowing the femur to be easily translated and reduced laterally over the tibial plateau. The medial collateral ligament (MCL) was torn at its femoral attachment, and the anterior cruciate ligament were ruptured but the posterior cruciate ligament was intact. The MPFL and vastus medialis rent was reapproximated with Ethibond 5. The medial retinaculum was imbricated over the repair with Vicryl 1 to reinforce the repair. The incision was then closed in layers in the usual fashion. Postoperative pulses were strong on the operated limb and postoperative ABI was 1.34 and 1.28 for the posterior tibial and dorsalis pedis pulses on the operated side, respectively, and 1.3 and 1.25 for the contralateral, non-operated side, respectively.

His knee pain resolved completely after surgery and compartments remained soft. He was allowed to bear weight as tolerated in a hinged knee brace locked in extension for 6 wk postoperatively. At 6-wk follow-up, he was ambulating independently in the knee brace and the surgical incision had healed completely.

DISCUSSION

Posterolateral dislocations of the knee are uncommon entities. They can arise from very low energy trauma comprising a valgus moment to a slightly flexed knee, with the tibia rotating relative to the femur. The exact direction of rotation of the tibia relative to the femur is subject to debate^[1,3]. An axial load is then necessary to allow the medial femoral condyle to buttonhole through the adjacent soft tissue^[1]. The key to managing these injuries is to recognize that closed reduction may not be possible, and the patient should be brought to the operating room as soon as is reasonably possible for an open reduction.

The pathognomonic sign of a posterolateral knee dislocation is the anteromedial distal thigh transverse "pucker" or "dimple sign". While this is immediately obvious with the knee in extension, the anteromedial "pucker" is accentuated by flexion. This is because the medial retinaculum, vastus medialis and MPFL tissue normally translate proximally with knee flexion. With the tissue trapped in the intercondylar notch, proximal translation is not possible and soft tissue attachments invaginate the skin inwards towards the intercondylar notch during flexion, making the "pucker" more prominent (Figure 3). To avoid discomfort, we recommend that knee flexion only be attempted under anesthesia. Another pathognomonic sign is the presence of the medial femoral condyle in the immediate subcutaneous location as a smooth, bony prominence proximal to the "pucker", almost "tenting" the skin. This is because all adjacent soft tissue (capsule, MPFL, vastus medialis, medial retinaculum) has receded around the condyle, allowing it to buttonhole through the tissue and come into prominence. Again, this is accentuated by knee flexion. Similar to other types of knee dislocation, determining the range of motion of an unreduced knee



Figure 1 Clinical photograph showing the “pucker” sign with the knee in extension.

at presentation is unnecessary.

Radiographs are also pathognomonic of a posterolateral knee dislocation. Much like rotatory dislocations of the proximal phalangeal joint of the finger, radiographs of a posterolateral knee dislocation will not reveal a true anteroposterior (AP) or lateral view of both the tibia and the femur in any single radiograph. An additional telltale sign is the view of the patella. This is because the patella maintains its in-line attachments to the tibial tuberosity (patellar tendon and quadriceps tendon) and will appear reduced with respect to the proximal tibia, but dislocated with respect to the distal femur. Thus, an AP radiograph of the knee will likely demonstrate an AP of the proximal tibia and an oblique of the distal femur (Figure 2A). Because the AP radiograph is shot directly over the patella with the patella facing the ceiling, the patella will appear in an AP projection also. In addition, medial opening of the tibiofemoral joint is noted, suggestive of medial soft tissue interposition^[1]. Similarly, a lateral radiograph of the knee will show a lateral of the proximal tibia and patella, but an oblique of the femur (Figure 2B). An effusion is usually appreciated on the lateral projection as well^[4], however in our patient, this was replaced by diffuse soft tissue swelling of the entire limb because of the interval to presentation. An oblique projection will appear to show apparent patella dislocation relative to the femur (Figure 2C).

Similar to other types of knee dislocations, ensuring distal limb viability and preservation of vascularity is of utmost importance. Evaluation of preoperative ABI will allow stratification for further vascular evaluation, and possible skeletal immobilization and vascular exploration, if necessary. It also provides a valuable baseline reading for comparison postoperatively. In a prospective study of 38 knee dislocations, Mills *et al*^[5] found that ABIs < 0.9 had sensitivity, specificity, positive predictive value of 100% and ABI > 0.9 had negative predictive value of 100% for arterial injury necessitating surgical intervention. While some authors perform computed tomography angiograms routinely for posterolateral knee dislocation (Table 1)^[2,4], we believe that in the presence of palpable pulses, a warm foot and normal ABIs, further vascular imaging is but an unnecessary delay. In a

review of reports of posterolateral knee dislocations, only 1 author reported loss of pulses (Table 1). This was because of a high-energy dislocation.

Some authors advocate magnetic resonance imaging (MRI) (Table 1)^[2,4] to demonstrate torn structures interposed in the intercondylar notch, evaluate the integrity of the cruciate and collateral ligaments, and demonstrate the pathognomonic MR “dimple sign”^[6]. We feel that these findings are equally easily discerned following the skin incision. An urgent MRI does not alter surgical management acutely, and urgent surgical reduction should take priority. Further, the distorted anatomy of an unreduced knee may also impair the diagnostic accuracy of MRI. While cruciate ligament ruptures may be picked up on MRI, these need not be addressed in the emergent setting^[2]. Should the patient present with late symptoms or persistent instability in the postoperative period after a period of soft tissue healing, the cruciate ligaments can be easily evaluated with an MRI at that time.

Unlike other permutations of knee dislocation, closed reduction of posterolateral knee dislocation is rarely possible. While some authors advocate attempting a closed reduction (Table 1)^[1,7-9], we feel that these attempts are both uncomfortable and unnecessary and serve only to increase the prominence of soft tissue puckering and jeopardize the viability of the already tenuous soft tissue envelope^[1], and delay surgical management. Similar to other dislocations involving buttonholing of bony prominences through soft tissue, the classic reduction maneuver of in-line traction functions only to tighten torn tissue around the condylar expansion.

Some authors attempt arthroscopic- or arthroscopic-assisted reduction prior to open reduction, both in an attempt to spare the patient a disfiguring incision, and to allow for closer intra-articular inspection^[1]. There are some limitations to this approach. Normal bony anatomy is distorted, making localization of the usual arthroscopic portals difficult. Because of capsular rupture, containment of insufflation fluid is not possible, leading to progressive extravasation, aggravating existing soft tissue edema and swelling, potentially increasing intracompartmental pressures. Entrapped tissue in the intercondylar notch is often on tension, and cannot be extricated by an arthroscopic probe alone^[1]. Further, it is not possible to reapproximate torn medial structures arthroscopically, and a final extensile medial incision is inevitable.

Surgical reduction should be performed emergently to reduce the risk of skin necrosis at the point of maximal invagination and tethering^[1,2]. The surgical technique for open reduction is not difficult. The surgical approach is extensile and direct, and targeted at achieving maximal exposure of torn structures and the buttonholed medial femoral condyle. Following division or reduction of the interposed tissue, reduction is achieved almost instantaneously by translating the femur laterally with minimal effort. These soft tissues can include medial capsule, retinaculum, MCL, MPFL, vastus medialis and medial meniscus. Division of interposed tissue may be necessary

Table 1 Characteristics of reported cases of posterolateral dislocation of the knee

Ref.	Patient age and gender	Torn structures (besides medial capsule, retinaculum, vastus medialis, MPFL)	MRI	Doppler	Angiogram/CT angiogram	Attempted closed reduction	Arthroscopic surgery	Interval to open reduction	Open surgery
Current study	48 M	MCL, ACL	No	Yes	No	No	No	4 h	Yes
Nystrom <i>et al</i> ^[8]	24 M and 31 F	MCL, ACL, PCL	No	No	No	Yes	No	Not mentioned	Yes
Huang <i>et al</i> ^[1]	61 M	ACL, PCL, MCL (also degenerative arthrosis)	No	No	No	Yes	Yes	> 8 h	Yes
Jeevanavar <i>et al</i> ^[2]	32 M	MCL, medial retinaculum, partial ACL tear	Yes	Yes	Yes	Yes	No	Not mentioned	Yes
Paulin <i>et al</i> ^[4]	54 M	ACL, PCL, MCL, LCL	Yes	No	Yes	Yes	No	< 24 h	Yes
Quinlan <i>et al</i> ^[3]	38 M, 40 F, 49 M, 20 M, 41 F	ACL, PCL, MCL in all patients, additional medial meniscus tear in 1 patient	No	No	No	3 of 5 cases	No	24 h in 4 cases, few days later in 1 case	Yes
Ashkan <i>et al</i> ^[7]	37 M	ACL, PCL, MCL, LCL, PLC	No	No	No	Yes	No	Following thoracoabdominal surgery	Yes
Urgüden <i>et al</i> ^[9]	51 M and 53 F	Medial retinaculum, MCL, ACL, PCL	No	Yes in 1 patient	No	Yes	No	4 h in both	Yes

ACL: Anterior cruciate ligament; PCL: Posterior cruciate ligament; MCL: Medial collateral ligament; LCL: Lateral collateral ligament; PLC: Posterolateral corner; MPFL: Medial patellofemoral ligament; M: Male; F: Female; MRI: Magnetic resonance imaging; CT: Computed tomography.

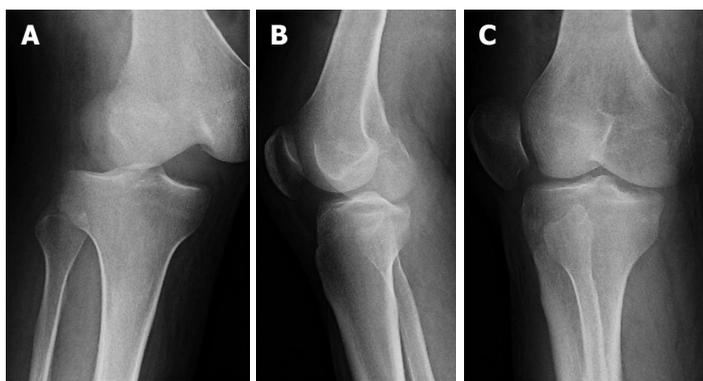


Figure 2 Supine radiographs showing posterolateral dislocation of the knee. A: AP; B: Lateral; C: Oblique. Note similar projections (AP or lateral) of both the tibia and femur are not seen in any single view. AP: Anteroposterior.



Figure 3 Clinical photograph under anesthesia showing accentuation of the “pucker” sign (black arrow) with flexion of the knee.

if there is tight contracture, especially in late-presenting cases.

Postoperatively, the knee is protected in a hinged knee brace during mobilization. Besides torn medial

structures and cruciate ligaments, some authors have found avulsion of lateral structures including the lateral collateral ligament from its femoral attachment^[4]. Protected weight-bearing will allow for healing of torn, repaired and reapproximated structures. Long term follow-up is necessary to detect the onset of post-traumatic arthritis.

Posterolateral dislocations of the knee are uncommon entities. Early recognition is key. Pathognomonic findings include the anteromedial “pucker” sign that is accentuated by knee flexion, and characteristic radiographs that do not show the same projections of the long bones in any single view. Attempting closed reduction will not be a rewarding endeavor. Instead, open reduction should be performed as soon as vascular compromise is excluded. MRI is not crucial in the preoperative period and can lead to delays of up to 24 h and can compromise the overlying soft tissue envelope^[4]. MRI can be obtained postoperatively following a period of soft tissue healing in patients with persistent symptoms.

COMMENTS

Case characteristics

A 48-year-old man presented with right knee pain and swelling 3 d after twisting his right knee during a fall.

Clinical diagnosis

Gross swelling of the right thigh to ankle with distal thigh blistering. "Pucker" sign was visible over the distal anteromedial thigh. Subcutaneous bony prominence (medial femoral condyle) was palpable proximal to the pucker. Pulses were strong and ankle-brachial index was > 1.0 bilaterally.

Differential diagnosis

Knee septic arthritis, knee effusion, deep vein thrombosis, compartment syndrome, anterior knee dislocation, posterior knee dislocation, cruciate or collateral ligament injury, tumor.

Laboratory diagnosis

All labs within normal limits.

Imaging diagnosis

Radiographs revealed posterolateral dislocation of the knee.

Pathological diagnosis

Posterolateral dislocation of the knee.

Treatment

Operative open reduction and repair of medial retinaculum, medial patello-femoral ligament and vastus medialis.

Related reports

Posterolateral knee dislocations are uncommon and can be missed. Magnetic resonance imaging (MRI) will only delay treatment. Closed reduction may not be possible. Urgent open reduction is necessary to preserve the tenuous soft tissue envelope.

Experiences and lessons

This condition is uncommon. Urgent open reduction is often necessary as closed

reduction is usually impossible. MRI in the acute setting will only serve to delay open reduction and will not guide immediate management.

Peer-review

The authors reported a rare case of posterolateral dislocations of the knee. It is a well written case report.

REFERENCES

- 1 **Huang FS**, Simonian PT, Chansky HA. Irreducible posterolateral dislocation of the knee. *Arthroscopy* 2000; **16**: 323-327 [PMID: 10750013 DOI: 10.1016/S0749-8063(00)90057-4]
- 2 **Jeevannavar SS**, Shettar CM. 'Pucker sign' an indicator of irreducible knee dislocation. *BMJ Case Rep* 2013; **2013**: pii: bcr2013201279 [PMID: 24096095 DOI: 10.1136/bcr-2013-201279]
- 3 **Quinlan AG**, Sharrard WJ. Postero-lateral dislocation of the knee with capsular interposition. *J Bone Joint Surg Br* 1958; **40-B**: 660-663 [PMID: 13610979]
- 4 **Paulin E**, Boudabbous S, Nicodème JD, Arditi D, Becker C. Radiological assessment of irreducible posterolateral knee subluxation after dislocation due to interposition of the vastus medialis: a case report. *Skeletal Radiol* 2015; **44**: 883-888 [PMID: 25560996 DOI: 10.1007/s00256-014-2085-1]
- 5 **Mills WJ**, Barei DP, McNair P. The value of the ankle-brachial index for diagnosing arterial injury after knee dislocation: a prospective study. *J Trauma* 2004; **56**: 1261-1265 [PMID: 15211135 DOI: 10.1097/01.TA.0000068995.63201.0B]
- 6 **Harb A**, Lincoln D, Michaelson J. The MR dimple sign in irreducible posterolateral knee dislocations. *Skeletal Radiol* 2009; **38**: 1111-1114 [PMID: 19543725 DOI: 10.1007/s00256-009-0729-3]
- 7 **Ashkan K**, Shelly RW, Barlow IW. An unusual case of irreducible knee dislocation. *Injury* 1998; **29**: 383-384 [PMID: 9813685 DOI: 10.1016/S0020-1383(97)00213-1]
- 8 **Nystrom M**, Samimi S, Ha'Eri GB. Two cases of irreducible knee dislocation occurring simultaneously in two patients and a review of the literature. *Clin Orthop Relat Res* 1992; **277**: 197-200 [PMID: 1555342 DOI: 10.1097/00003086-199204000-00024]
- 9 **Urgüden M**, Bilbaşar H, Ozenci AM, Akyıldız FF, Gür S. Irreducible posterolateral knee dislocation resulting from a low-energy trauma. *Arthroscopy* 2004; **20** Suppl 2: 50-53 [PMID: 15243425]

P- Reviewer: Knutsen G, Martinelli N, Zheng N
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 July 18; 7(7): 406-462



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srecko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*



REVIEW

- 406 Prenatal diagnosis and assessment of congenital spinal anomalies: Review for prenatal counseling
Upasani VV, Ketwaroo PD, Estroff JA, Warf BC, Emans JB, Glotzbecker MP

ORIGINAL ARTICLE

Basic Study

- 418 Evaluation of bone remodeling in regard to the age of scaphoid non-unions
Rein S, Hanisch U, Schaller HE, Zwipp H, Rammelt S, Weindel S

Case Control Study

- 426 Computerized tomography based "patient specific blocks" improve postoperative mechanical alignment in primary total knee arthroplasty
Vaishya R, Vijay V, Birla VP, Agarwal AK

Retrospective Cohort Study

- 434 Constrained fixed-fulcrum reverse shoulder arthroplasty improves functional outcome in epileptic patients with recurrent shoulder instability
Thangarajah T, Higgs D, Bayley JIL, Lambert SM

Retrospective Study

- 442 Trochanter/calcar preserving reconstruction in tumors involving the femoral head and neck
Cho HS, Lee YK, Ha YC, Koo KH

CASE REPORT

- 448 Extensor pollicis brevis tendon can hyperextend thumb interphalangeal joint in absence of extensor pollicis longus: Case report and review of the literature
Strauch RJ, Strauch CB
- 452 Hemorrhagic lumbar synovial facet cyst secondary to transforaminal epidural injection: A case report and review of the literature
Elgafy H, Peters N, Lea JE, Wetzel RM
- 458 Operative stabilization of the remaining mobile segment in ankylosed cervical spine in systemic onset - juvenile idiopathic arthritis: A case report
Suhodolčan L, Mihelak M, Brecej J, Vengust R

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Nathan Joseph Fanter, MD, Attending Doctor, Surgeon, Department of Orthopaedic Surgery, Edward Hines Jr. VA Hospital, Hines, IL 60141, United States

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthritis, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Huan-Liang Wu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center, No. 62 Dongsihuan Zhonglu, Chaoyang District, Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

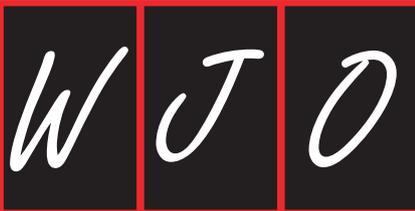
PUBLICATION DATE
 July 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
 Full instructions are available online at http://www.wjnet.com/bpg/g_info_20160116143427.htm

ONLINE SUBMISSION
<http://www.wjnet.com/esps/>



Prenatal diagnosis and assessment of congenital spinal anomalies: Review for prenatal counseling

Vidyadhar V Upasani, Pamela Deaver Ketwaroo, Judy A Estroff, Benjamin C Warf, John B Emans, Michael P Glotzbecker

Vidyadhar V Upasani, Department of Orthopedic Surgery, Rady Children's Hospital San Diego, San Diego, CA 92123, United States

Pamela Deaver Ketwaroo, Department of Radiology, Brigham and Women's Hospital, Boston, MA 02115, United States

Judy A Estroff, Department of Radiology, Boston Children's Hospital, Boston, MA 02115, United States

Benjamin C Warf, Department of Neurosurgery, Boston Children's Hospital, Boston, MA 02115, United States

John B Emans, Michael P Glotzbecker, Department of Orthopedic Surgery, Boston Children's Hospital, Boston, MA 02115, United States

Author contributions: Upasani VV, Ketwaroo PD and Glotzbecker MP contributed to patient chart review, manuscript preparation, manuscript editing; Estroff JA, Warf BC and Emans JB contributed to manuscript preparation, manuscript editing.

Conflict-of-interest statement: None of the authors on this manuscript have any direct or indirect conflicts of interest or financial disclosures related to the contents of this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Vidyadhar V Upasani, MD, Assistant Clinical Professor, Department of Orthopedic Surgery, Rady Children's Hospital San Diego, 3030 Children's Way, Suite 410, San Diego, CA 92123, United States. vupasani@rchsd.org
Telephone: +1-858-9666789
Fax: +1-858-9668519

Received: February 3, 2016

Peer-review started: February 14, 2016

First decision: March 21, 2016

Revised: May 3, 2016

Accepted: May 31, 2016

Article in press: June 2, 2016

Published online: July 18, 2016

Abstract

The last two decades have seen continuous advances in prenatal ultrasonography and *in utero* magnetic resonance imaging. These technologies have increasingly enabled the identification of various spinal pathologies during early stages of gestation. The purpose of this paper is to review the range of fetal spine anomalies and their management, with the goal of improving the clinician's ability to counsel expectant parents prenatally.

Key words: Prenatal ultrasound; *In utero* magnetic resonance imaging; Prenatal counseling; Congenital spinal anomalies

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Advances in prenatal ultrasonography and *in utero* magnetic resonance imaging have given clinicians powerful tools to identify spinal pathologies during early stages of gestation. Prenatal counseling requires a "team" of appropriate specialists requiring coordination and cross-communication from multiple surgical and medical disciplines. The orthopedic clinician should critically assess the accuracy of the diagnosis, the likely natural history of the deformity, what treatments may be required, and what the impact of the anomaly will be on the child's growth and eventual adult function.

Upasani VV, Ketwaroo PD, Estroff JA, Warf BC, Emans JB, Glotzbecker MP. Prenatal diagnosis and assessment of congenital spinal anomalies: Review for prenatal counseling. *World J Orthop* 2016; 7(7): 406-417 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/406.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.406>

INTRODUCTION

The last two decades have seen continuous advances in prenatal ultrasonography and *in utero* magnetic resonance imaging (MRI). These technologies have increasingly enabled the identification of various spinal pathologies during early stages of gestation. The purpose of this paper is to review the range of fetal spine anomalies and their management, with the goal of improving the clinician's ability to counsel expectant parents prenatally.

PRENATAL COUNSELING

The interdependent roles of radiologist and counseling clinicians

The availability of detailed information about skeletal and visceral anomalies allows more accurate fetal diagnosis but also renders the job of the counseling clinicians more complex. Because so many skeletal anomalies are associated with either other anomalies or genetic syndromes, prenatal counseling requires a "team" of appropriate specialists. Armed with prenatal imaging, counseling clinicians are obligated not just to give the family their best estimate of a diagnosis, but also to put the fetus's condition into perspective and attempt to provide some over-arching outlook for the family. This may require coordination and cross-communication among specialists from multiple surgical and medical disciplines. Faced with a fetal spine anomaly, the clinician should critically assess the accuracy of the diagnosis, the likely natural history of the deformity, what treatments are likely, and what the impact of the anomaly will be on the child's growth and eventual adult functioning. This estimate will be easy for an isolated hemivertebra but becomes more complex for multiple vertebral anomalies, spinal dysraphism, myelodysplasia or segmental spinal dysgenesis. Experience with the accuracy of previous prenatal diagnoses makes a more accurate prognosis possible. Co-consultation with other medical or surgical specialists is critical when more than one organ system is involved.

IMAGING PRINCIPLES

Prenatal 2-D and 3-D ultrasound for spinal anomaly detection

While some anomalies in the spina bifida spectrum

result in open neural tube defects and therefore may be initially detected with elevated maternal serum alpha fetoprotein, skin covered (closed) spinal dysraphism and other spinal anomalies such as diastematomyelia, vertebral segmentation anomalies, sacral agenesis, spinal dysgenesis, spondylothoracic or spondylocostal dysplasia, or some skeletal dysplasias may be detected only by prenatal imaging. Routine fetal sonography has not been mandated in the United States; however, most pregnant women have at least one detailed anatomical evaluation usually occurring between 18-24 wk of gestation. More recently, routine first trimester ultrasound and maternal serum screening has been offered to patients between 11 and 14 wk of gestation with the goal of measuring the fetal nuchal translucency thickness, nasal bone length and ductus venosus waveform. Imaging at this early time point in the hands of an experienced practitioner may allow for detection of fetal structural anomalies, such as neural tube defects^[1]. One metric that has been used in this timeframe is biparietal diameter, which has been shown to measure less than the 5th percentile in 50% of spina bifida patients^[1].

Neural element involvement in cases of spinal dysraphism may only be detectable by ultrasound with a high frequency linear transducer^[2]. However, more typical obstetrical ultrasound transducers (6-8 MHz) may still detect neural tube defects or abnormal limb positioning, which can serve as an early indicator of neurological dysfunction. Three-dimensional ultrasound of the fetal spine can have great diagnostic benefit, as it allows the operator to manipulate data in any plane after the completion of the exam, particularly if fetal positioning during the optimized 2-D acquisition is challenging^[2]. In many cases, however, the presence of the obligatory cranial anomalies associated with an open neural tube defect, described in further detail below, are more readily observed than the spinal defect itself. In general, ultrasonography is able to detect vertebral segmentation, laminar segmentation or rib developmental anomalies as well as gross alignment abnormalities. Congenital fusion or spinal stenosis on the other hand may be better appreciated with MRI.

Prenatal MRI of spinal anomalies

MRI can be used prenatally to better delineate involvement of neural elements associated with osseous spinal anomalies^[3]. This can be important for delivery planning, decisions regarding pregnancy interruption, and in some cases, preparation for *in utero* surgery. Patients with closed neural tube defects have a better postnatal prognosis, including superior bladder functionality and lower risk of scoliosis, than their open neural tube defect counterparts, and MRI may more clearly distinguish these two populations^[2,4]. While it is not typically utilized for screening purposes, in some cases, fetal MRI may also demonstrate unsuspected spinal anomalies in

fetuses imaged for evaluation of other organ systems.

Fetal MRI provides superior soft tissue contrast. However, fetal movement can make MR imaging in standard planes challenging, and fast pulse sequences such as steady state free precession, half-fourier acquisition single-shot turbo spin echo, fast T1-weighted gradient echo, and echo planar imaging are often utilized. Thin slices of 2-4 mm thickness can minimize the detrimental effects of fetal movement on image quality while maximizing detail of the spinal and cranial anomalies^[2,3]. Standard fetal MRI is performed at 1.5 or 3 Tesla field strength. Gadolinium-based contrast agents are not administered to pregnant women, given their ability to cross the placenta and the potential toxicity of unchelated gadolinium to the developing fetus^[5]. MRI can be used to approximate the location of the conus, and identify a lipoma or other soft tissue mass within the spine, however can often not detect a syrinx, fatty filum or be used to assess spinal alignment.

Postnatal imaging of spinal anomalies

Additional imaging in the postnatal period can be useful in evaluating the newborn with vertebral anomalies noted on pre-natal imaging. Plain radiographs (AP and lateral of the entire spine including the ribs), should be obtained early, optimally in the first 2 mo, as the bony details of a prenatally-noted anomaly are more evident before further ossification of the vertebra, and other anomalies not seen prenatally can sometimes be detected. All congenital vertebral anomalies have an increased risk (approximately 15%) of intraspinal anomalies. Neonatal spinal ultrasound performed before extensive laminar ossification has occurred (6-12 wk) will show major intraspinal anomalies and tethering^[6]. MRI of course better demonstrates intraspinal anomalies^[7-9], but generally requires a general anesthetic or heavy sedation which has theoretical deleterious effects in the young child^[10-12]. MR can sometimes be accomplished with a "feed and wrap" technique in the infant without general anesthesia or sedation. This technique is used to soothe the child in an attempt to obtain the imaging without requiring sedation. When and whether all vertebral anomalies should be evaluated postnatally with MRI for intraspinal anomalies is debated. Certainly any patient with clinical signs of intraspinal anomaly (extremity deformity or bladder function suggestive of neurologic abnormality) or about to have surgery of the spine should have a whole spine MR. Otherwise the MR may be deferred until an older age when easier to perform or may possibly never be needed if the anomaly is minor without neurologic symptoms. Evaluation of the neonatal spine is typically performed with ultrasound and radiography, though MRI sometimes plays a role as well. While radiographs may readily identify bony abnormalities in the case of vertebral segmentation or formation, ultrasound or MRI better assesses the relationship to neural elements.

CONGENITAL SPINAL ANOMALIES

Chiari malformation

Chiari malformations (CM) describe a heterogeneous group of conditions that are likely embryologically unrelated. Types I and II CM both involve displacement of the cerebellum with (type II) or without (type I) displacement of the lower brainstem caudal to the foramen magnum^[13]. The resulting compression of these structures can affect neurologic function and impede the normal flow of cerebrospinal fluid. CM type II is thought to be due to intrinsic structural anomalies of the brain and spinal cord during fetal development in relation to an accompanying neural tube defect^[14,15]. Genetic, nutritional, and environmental factors have all been demonstrated to play a role in the evolution of these defects.

Type I CM involves extension of the cerebellar tonsils into the foramen magnum and may be discovered incidentally, often later in childhood or even adulthood and often does not require further treatment. Type II CM (previously referred to as Arnold-Chiari malformation) is certainly the more commonly diagnosed prenatal condition of the two. Affected fetuses have a small posterior fossa with hindbrain malformation consisting of displacement of the lower brainstem and cerebellar tonsils and vermis through an enlarged foramen magnum, tectal beaking, medullary kink, enlarged massa intermedia, callosal dysgenesis, and towering cerebellum through an enlarged tentorial hiatus^[16,17]. This is almost always found in association with a myelomeningocele. Chiari III malformation is serious though fortunately rare and may be diagnosed prenatally after identification of an occipital encephalocele containing herniated cerebellum in addition to the findings of Chiari II. Chiari IV malformation is also extremely rare and demonstrates cerebellar hypoplasia with normal positioning of the cerebellar tonsils.

Prenatal findings: Ultrasonographic identification of CM *in utero* can provide valuable information regarding associated conditions. For example, ventriculomegaly is the most common prenatal finding associated with Type II CM and can be associated with neurologic dysfunction, structural abnormalities of the skull, and poor fetal outcome. Biconcave frontal bones resulting in the "lemon sign" on ultrasound (Figure 1) are often seen, though are not specific to an open neural tube defect; 1%-2% of normal fetuses may have this finding, and it may resolve over time even in patients with open neural tube defects^[2]. Curved, diminutive appearance of the cerebellum due to effacement of the cisterna magna results in the typical "banana sign" on ultrasound (Figure 2), which has higher specificity for the diagnosis and is 99% sensitive. When combined, the lemon and banana signs have a > 99% sensitivity for CM type II prenatally^[16]. In addition, there is an almost invariable

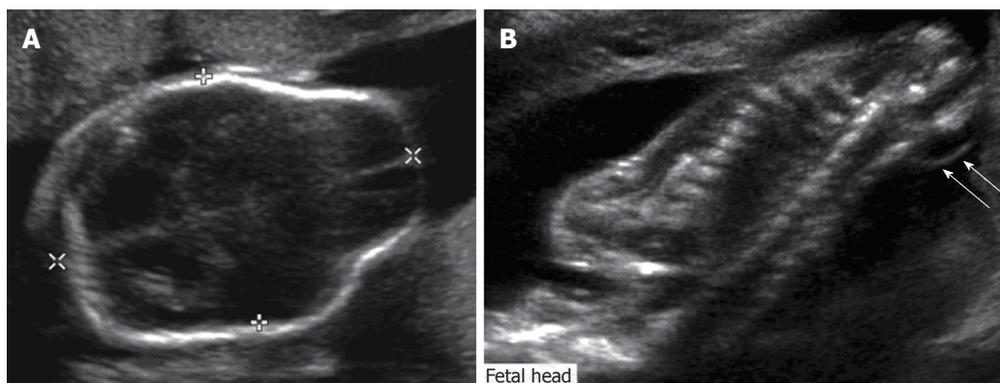


Figure 1 Fetal ultrasound. Grayscale ultrasound images of the fetal head (A) and spine (B) demonstrate ventriculomegaly as well as a lemon-shaped configuration of the fetal head due to bifrontal concavity, typical of Chiari II malformation. There is an associated myelomeningocele (arrows).

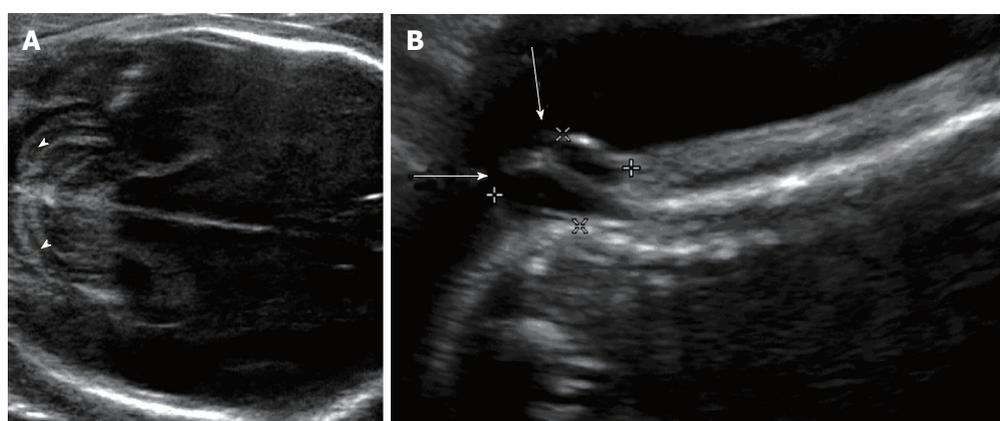


Figure 2 Chiari ultrasound. Grayscale ultrasound images of the 23 wk fetal head (A) and spine (B) demonstrate curved, “banana-shaped” appearance of the fetal cerebellum (arrowheads) typical of Chiari II malformation, as well as associated lower sacral myelomeningocele (arrows).

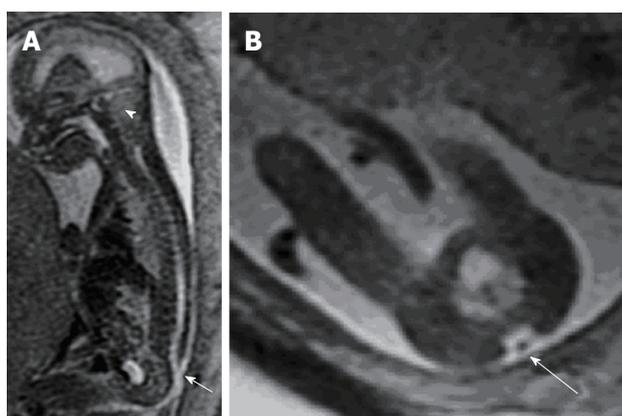


Figure 3 Fetal magnetic resonance imaging. A: Sagittal T2 weighted fetal MR demonstrates a small posterior fossa (arrowhead) with crowding of the cerebellar tonsils and hindbrain; B: Evaluation of the spine demonstrated a lumbosacral myelomeningocele.

association with myelomeningocele. While CM type II is typically diagnosed with prenatal ultrasound, fetal MRI (Figure 3) allows for confirmation, further evaluation if ultrasound is technically limited, and evaluation of associated intracranial findings such as callosal agenesis and hydrocephalus^[18].

Postnatal evaluation and treatment: For all types of CM, findings are usually first diagnosed with MRI, which demonstrates the classic findings described above. Neurosurgical consultation is warranted in patients with CM to consider decompression of the hindbrain or treatment for hydrocephalus. Intervention for Chiari type I in the infant should generally not be entertained without a compelling clinical indication, such as lower cranial nerve dysfunction (*e.g.*, apnea or dysphagia) or hydromyelia (syringomyelia). Such is uncommon in young infants. The classic symptoms, suboccipital and posterior neck pain exacerbated by activities involving a valsalva maneuver, cannot be appreciated in babies, and in very young children operative intervention for pain symptoms alone should be approached with caution. This is a dynamic malformation resulting from a relative deficit in the posterior fossa volume, which can change with further growth and development. In other words, for very young children, the malformation can resolve spontaneously over time. Furthermore, infants undergoing posterior fossa decompression for Chiari are more likely to have recurrence from scarring and bone regrowth, requiring repeat surgery in the future.

Patients with Chiari I malformation can present with hydromyelia (syringomyelia) even without other



Figure 4 Myelomeningocele magnetic resonance - T2 weighted magnetic resonance image of a 26 wk fetus demonstrates a large thoracolumbar myelomeningocele (arrows) covered by skin.

symptoms. Hydromyelia, or expansion of the central canal of the spinal cord (not unlike the ventriculomegaly of hydrocephalus), results from disturbed CSF flow and pulsatility at the level of the craniocervical junction in these patients. This commonly presents as progressive scoliosis, which is often “atypical” (*e.g.*, levoscoliosis, young age, or male gender), and the diagnosis is made by MRI as part of the scoliosis workup. Chiari decompression (suboccipital craniectomy, C1 laminectomy, and duraplasty) results in resolution of the hydromyelia in most cases. If the scoliosis is not yet severe, the curve progression can be arrested or even reversed without orthopedic intervention. Untreated Chiari I with hydromyelia can lead to indolently progressive neurological deterioration involving both upper and lower motor neuronal dysfunction.

Infants with myelomeningocele and the type II Chiari malformation are quite distinct from those with Chiari I. The latter is rarely associated with hydrocephalus, while the former most commonly is. Furthermore, the type II malformation involves more than mechanical constriction of the hindbrain structures. This is a diffuse neuronal migrational anomaly affecting the entire central nervous system, with implications for neurocognitive and motor development in addition to the possibility of intrinsic brainstem dysfunction apart from the effects of mechanical compression.

The initial approach to treating symptoms of hindbrain dysfunction (*e.g.*, stridor, dysphagia, apnea) or expanding hydromyelia in these infants is treatment of the accompanying hydrocephalus, which can now often be successfully accomplished endoscopically without shunt implantation^[19,20]. Only when this has been satisfactorily accomplished should hindbrain decompression be considered, and at times recovery of lower cranial nerve functions is not realized even with that intervention.

In contrast to the Chiari I malformation, infants with Chiari II have an enlarged foramen magnum and the torcular and transverse sinuses are typically very low-

lying. Hence, the need for suboccipital craniectomy is minimal and associated with higher risk, and the key part of the decompression is comprised of cervical laminectomies and an expansion duraplasty for dorsal decompression of the hindbrain seated in the cervical spinal canal.

Myelomeningocele

Myelomeningocele is a primary neural tube defect associated with failure of neural tube closure at some point along the developing spinal cord that results in a segmental spinal cord malformation with absence of the overlying dura, lamina, soft tissues and skin (Figure 4). There is typically a membrane covering the defect that traps the CSF^[18]. It is one of the most common spinal anomalies, with a worldwide incidence of 1 in 1000 births^[21]. A genetic predisposition to this condition has been identified in some cases, and supplemental maternal folic acid beginning prior to conception and extending through the first month of pregnancy decreases its incidence. Because of this, the incidence in a given population is variable depending on maternal access to prenatal care and nutrition in addition to genetic factors.

The laminar defect, referred to as spina bifida, can also be seen in isolation or in the context of other skin covered anomalies of the spinal cord (Figure 5). These are often referred to as “spina bifida occulta” (as opposed to the “spina bifida aperta” of myelomeningocele). Spina bifida occulta lesions, such as filum lipoma, lipomyelomeningocele, and terminal myelocystocele are thought to be anomalies of “secondary neurulation” from errors in differentiation and migration of the caudal cell mass that occur after primary neurulation is complete. Thus, the general term, “spina bifida” is quite nonspecific, as is the term “dysraphism”, and can lead to confusion.

Prenatal findings: Myelomeningocele is often first suspected when routine screening during pregnancy reveals elevated levels of maternal serum alpha-fetoprotein^[22]. Targeted ultrasound also plays an important role in the early detection and delineation of neural tube defects. Myelomeningocele is virtually always accompanied by the Chiari II malformation, described above. Patients with myelomeningocele may have an additional spinal cord anomaly, such as a split cord malformation (diastematomyelia), warranting close attention to the spine in both pre- and post-natal populations for pre-surgical planning of myelomeningocele repair^[16].

Prenatal treatment: While early post-natal closure of the myelomeningocele to prevent infection is the gold standard, recent advances in fetal surgery have demonstrated that prenatal open or endoscopic repair of the neural tube defect may result in reversal of the Chiari II malformation, reduced incidence of

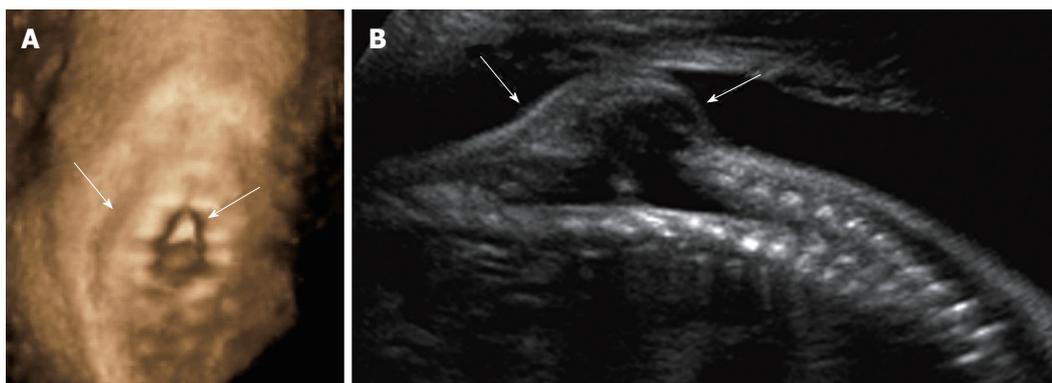


Figure 5 Spinal dysraphism ultrasound. Coronal 3D (A) and sagittal 2D (B) ultrasound images of the 26 wk fetal spine demonstrate dysraphism of the thoracolumbar junction (arrows), in the region of known myelomeningocele.

hydrocephalus, and slightly reduced severity of postnatal neurologic sequelae^[23,24]. The relative value of this intervention, however, must be considered within the context of maternal and fetal risk, including the risk of prematurity and its attendant sequelae, fetal demise, and uterine dehiscence. There also appears to be an increased risk of early symptomatic spinal cord tethering and intraspinal dermoid cyst formation. In general the prevalence of orthopedic manifestations of spina bifida, including gait abnormalities, foot deformities (equinovarus, cavovarus, calcaneovalgus, vertical talus), hip dislocations, and abnormalities in the rotational alignment of the lower extremities have not been significantly impacted by prenatal interventions^[21].

Postnatal evaluation and treatment: The most common early intervention aside from the initial myelomeningocele closure is the management of hydrocephalus, which is required in around two-thirds of the patients. Placement of a ventricular shunt had been the only effective treatment for these patients since the early 1960's; but, it has recently been demonstrated that the majority (around 75%) can be successfully treated with a minimally invasive endoscopic procedure that combines endoscopic third ventriculostomy with choroid plexus cauterization^[20,25].

The primary goals of orthopedic interventions should be to maximize function and mobility while minimizing deformity and pain. Treatment recommendations are based on the functional motor level of the lesion^[26,27]. In patients with a thoracic or upper lumbar functional level, the goals of treatment are to maintain spinal balance, a level pelvis, mobile hips and knees, and plantigrade feet. Most of these patients will require surgical stabilization of the spine to treat scoliosis and kyphosis^[28-31]. Patients with a mid-lumbar functional level usually have an intact quadriceps muscular function and have the potential to be limited community ambulators with braces and assistive devices. These patients often have weak hip abductors and develop significant genu valgum and knee flexion contractures.

Muscle transfers and osteotomies to correct coronal and axial plane abnormalities play an important role in keeping these patients ambulatory^[28,32]. Patients with low lumbar or high sacral function typically ambulate using ankle foot orthoses. Hip instability in this group should be aggressively managed to achieve concentric hip reduction and coverage^[33]. Foot reconstruction procedures to correct cavovarus deformity are indicated to maintain a supple foot that can be braced^[34,35].

Tethered spinal cord

Tethered spinal cord syndrome is a clinical entity in which spinal cord function is compromised by inappropriate attachment of and traction upon the cord, which appears to be associated with compromised tissue perfusion. Tethering of the cord is associated with a variety of etiologies, including scar formation from prior surgery (such as myelomeningocele repair) or an anomaly of secondary neurulation resulting in inappropriate conus traction from a filum lipoma or lipomyelomeningocele^[36,37]. Symptoms of spinal cord tethering may also result from a split cord malformation (diastematomyelia) or from a dermal sinus tract that extends intra-dural and is attached to the dorsal spinal cord.

Prenatal findings: *In utero* diagnosis of a tethered spinal cord is usually based on direct visualization of an abnormally caudal position of the conus medullaris, or by identification of a lipoma within the spinal canal. A low-lying conus terminates below the upper endplate of L3 in a child. Though normative values in the fetus have yet to be fully established, prenatal ultrasound has demonstrated that the conus has normally ascended to the L1/L2 level by the 40th postmenstrual week (Figure 6)^[38]. A tethering lesion may also result in lack of normal nerve root motion with the CSF pulsations during neonatal imaging. The diagnosis of tethered spinal cord can occasionally be made prenatally with ultrasound and fetal MRI, though postnatal diagnosis is far more common, and may be heralded by the

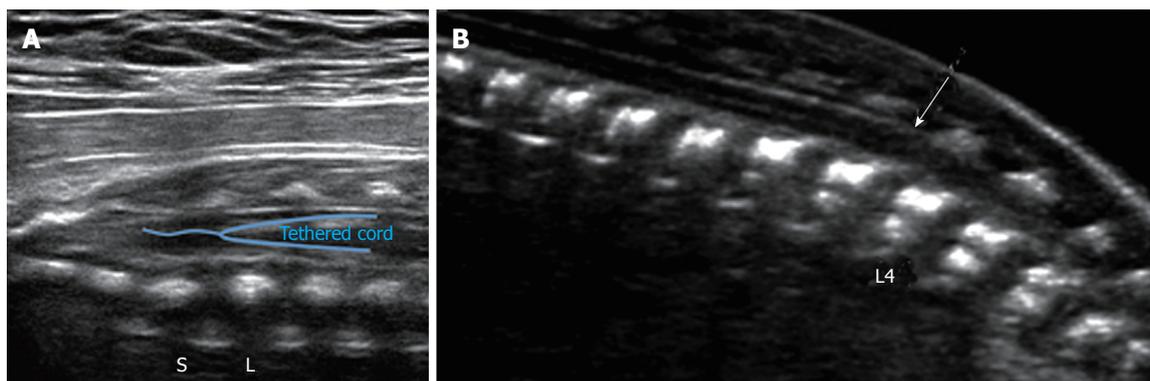


Figure 6 Spinal tether ultrasound. Grayscale ultrasound image (A) of the lumbosacral spine in a 29 wk fetus demonstrates a low-lying conus medullaris, extending below the lumbosacral junction (L/S). No evidence of associated fatty filum terminale was seen in this case; B: Grayscale ultrasound image of the lumbosacral spine in a 21 wk fetus demonstrates a low-lying conus medullaris (arrow), extending below the inferior endplate of L3. No evidence of associated fatty filum terminale was seen in this case.

presence of a sacral dimple or soft tissue mass, or after evaluation for symptoms related to cord tethering, such as bowel and bladder dysfunction, lower extremity orthopedic deformity, or ambulatory disturbance^[17].

Postnatal evaluation and treatment: Strictly speaking, “tethered spinal cord” is a clinical rather than radiological diagnosis, and the role of a radiologist is typically to identify possible reasons for clinical symptoms of tethering. Ultrasound can be used to identify tethering up to approximately 6 mo of age, though earlier imaging is technically easier when performed before the posterior spinal elements have ossified. If a spinal tether is not suspected until the child is older, MRI is required for diagnosis.

The clinical manifestations of tethering lesions due to abnormal traction on the conus vary^[39]. These include pain, neurogenic bladder dysfunction, progressive foot deformities, scoliosis, and the development of motor or sensory deficits in the lower extremities. It may be identified (as is also the case with hydromyelia) in cases where an MRI is ordered for a rapidly progressive or atypical scoliosis. The characteristic physical exam findings may include the presence of a hairy patch (associated with split cord malformations), sacral dimple, or subcutaneous lipoma in the lumbosacral region^[40].

Tethered spinal cord is often released surgically as a prophylactic measure in very young children because of the anticipated risk of progressive neurologic sequelae over time. In older children, symptomatic tethering of the spinal cord may occasionally be present even if the conus is normally positioned^[39], and a coexisting filum lipoma is often seen^[41]. Clinical indications for tether release include back or leg pain, progressive deterioration of motor or sensory function (such as a change in gait), neurogenic bladder dysfunction, constipation, progressive orthopedic deformities, or spasticity. Rarely, patients with dermal sinus tracts may develop recurrent meningitis^[42]. Although residual

deficits in urologic or neurologic function may persist, these patients can have an excellent quality of life. Patients with the recent onset of clinical manifestations such as pain, constipation, or urinary incontinence often experience resolution of their symptoms.

Diastematomyelia

Diastematomyelia is a rare congenital anomaly that results in a longitudinal split of the spinal cord^[43], usually occurring at the level of the upper lumbar vertebrae. The genesis of this anomaly is thought to occur very early in gestation during gastrulation and prior to neural tube closure. The two hemicords are typically separated by a fibrous, cartilaginous, or osseous septum and reside in two separate dural tubes (type I split cord malformation) (Figure 7). Type II split cord malformations have both hemicords within a single, non-duplicated, dural tube^[44]. Each hemicord usually contains a central canal, one dorsal horn and one ventral horn. The two hemicords typically reunite caudally, though two conus medullarum may be seen in diplomyelia, an embryologically distinct entity^[45]. Diastematomyelia is typically associated with vertebral segmental anomalies.

Prenatal findings: Though the diagnosis may go unrecognized by prenatal ultrasound in some cases, the presence of a septum between the two hemicords, which appears as an echogenic structure extending from the posterior elements to the posterior aspect of a vertebral body, has high specificity for diastematomyelia^[17,18,43]. The spinal canal may also be widened in the coronal plane^[41]. The mean gestational age at diagnosis is 21.5 wk, and approximately one third of patients have associated spinal dysraphism^[43]. Patients with isolated diastematomyelia have a far better postnatal prognosis than those with associated open neural tube defect, so identifying any of these findings prenatally is critical for family counseling. Prenatal MRI can be used to confirm the diagnosis and look for associated findings,

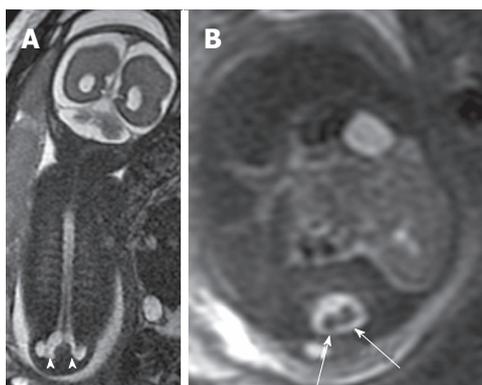


Figure 7 Lumbosacral myelomeningocele. Coronal (A) and axial (B) T2 weighted magnetic resonance images of a 26 wk fetus demonstrate complex spinal anomalies with a lumbosacral myelomeningocele (arrowheads) and diastematomyelia (arrows).

as some patients have associated meningocele or myelomeningocele, and 75% have tethering lesions^[17].

Postnatal evaluation and treatment: The clinical manifestations of diastematomyelia are very similar to those of a tethered cord. Cutaneous lesions, especially a patch of hypertrichosis, are often found over the affected area of the spine and the neurologic symptoms include motor or sensory deficits, scoliosis, incontinence and pain. Postnatal neurologic deficits may present as the child learns to walk, at which time evaluation with MRI is appropriate. MRI is used to confirm or make the diagnosis. In some cases, it may be found during screening MRI for early onset or atypical scoliosis.

If an associated myelomeningocele or secondary tethering lesion such as filum lipoma is not present, the role of prophylactic operative intervention is debated, but is certainly indicated for new or progressive symptoms. When indicated, surgical intervention includes decompression of the neural elements with excision of the interposing tissue and reconstruction of the duplicated dural sacs.

Vertebral formation/segmentation anomalies

Vertebrae typically develop between the sixth to eighth weeks of gestation when two lateral chondrification centers unite to form the primary ossification center of the vertebral body^[46]. A disruption in this process can lead to a failure of vertebral formation or segmentation (Figure 8). Although the exact etiology for this phenomenon is unknown, some attribute vertebral formation or segmentation anomalies to disruption of the vascular supply to that portion of the vertebral column^[47]. Vertebral anomalies may occur in multiple areas within the spine and are often associated with anomalies in the extremities and other organ systems, including cardiac, genitourinary, gastrointestinal, and pulmonary^[48]. They are broadly classified into categories including failure of formation or failure of segmentation.

Prenatal findings: Ultrasound can be used to detect

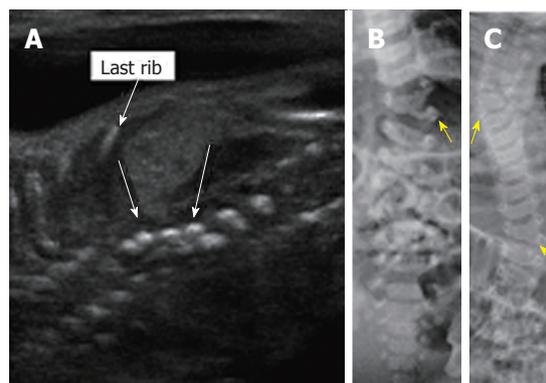


Figure 8 Thoracic hemivertebrae. Parasagittal grayscale ultrasound image (A) of a 20 wk fetus acquired with a high frequency linear transducer demonstrate unpaired echogenic structures at the thoracolumbar junction representing hemivertebrae (arrows). Postnatal frontal radiographs of the same patient's spine at 0 d (B) and 3 years of age (C) demonstrate left thoracolumbar and right midthoracic hemivertebrae.

a vertebral anomaly as early as the twelfth week of gestation^[49]. In particular, 3-D ultrasound can have a dramatic effect on ease of visualization of these lesions, particularly in skeletal rendering mode^[2]. Failures of formation, including hemivertebrae (Figure 9) and wedge vertebrae, may be identified with prenatal ultrasound or less commonly by MRI by recognizing abnormal spinal curvature and unpaired vertebral ossification centers. Failures of segmentation, including block vertebrae, unilateral bar vertebrae, and atlanto-occipital fusion are primarily related to failure of intervertebral disc formation and may present prenatally with fetal kyphoscoliosis^[50].

If a spine anomaly is identified, the lower extremities should be evaluated in detail for positioning and functionality. Identification of vertebral anomalies also warrants close inspection of the rest of the fetus, particularly to evaluate for VACTERL association [vertebral anomalies, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies/rib fusions (Figure 10), limb anomalies]^[16]. Amniocentesis can also provide valuable information regarding any chromosomal abnormalities that may be present.

Postnatal evaluation and treatment: Counseling and management of these patients depends on the gestational age at diagnosis, location and number of vertebral anomalies, and whether there is involvement of multiple organ systems. An isolated hemivertebra typically has a very good prognosis with conservative management and close follow-up. On the other hand, neonates with multiple vertebral anomalies as well as other organ system involvement are typically at higher risk for premature delivery and perinatal morbidity and mortality. Postnatal screening for associated intraspinal, cardiopulmonary, or urologic abnormalities is critical. In patients less than 3 mo of age, a spinal ultrasound may be used to identify a low-lying conus, diplomyelia, diastematomyelia or syringomyelia^[51]. Intraspinal

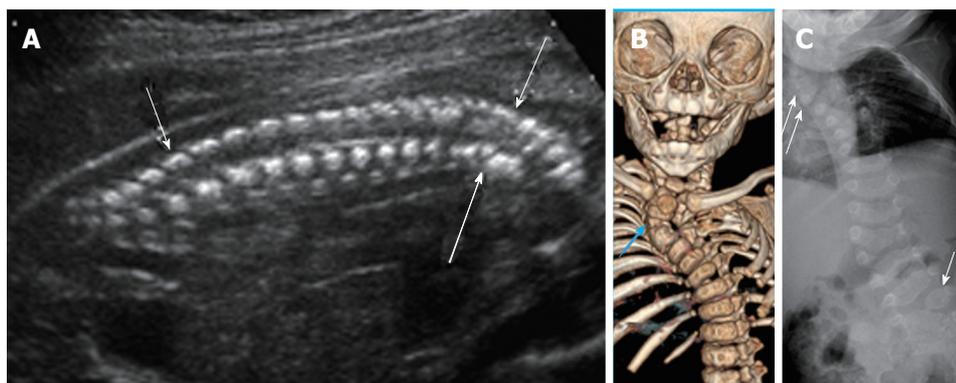


Figure 9 Cervicothoracic Hemivertebrae. Grayscale ultrasound image (A) of a 21 wk fetus demonstrate multiple hemivertebrae (arrows) and cervicothoracic kyphosis. Six months postnatal multidetector unenhanced computed tomography of the thorax with volume rendering (B) as well as frontal radiograph of the spine (C) demonstrate multiple vertebral segmentation anomalies, including right upper thoracic and left lumbosacral hemivertebrae (arrows), resulting in congenital cervicothoracic dextroscoliosis.

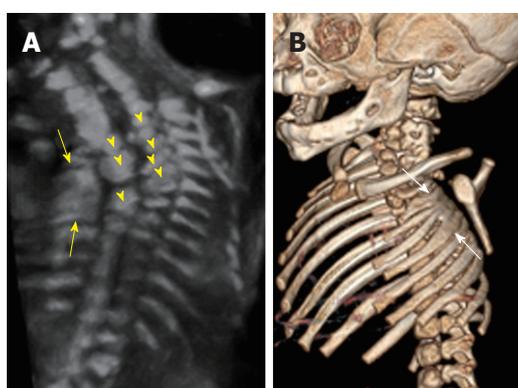


Figure 10 Rib fusions. Grayscale 3D ultrasound image (A) of a 21 wk fetus demonstrate fusion of multiple left sided ribs (arrows) as well as multiple segmentation anomalies (arrowheads) resulting in congenital cervicothoracic kyphoscoliosis. Postnatal multidetector unenhanced computed tomography (B) of the thorax with volume rendering demonstrates bony fusion of multiple left sided ribs (arrows) as well as multiple segmentation anomalies and cervicothoracic dextroscoliosis.

anomalies may be detected in up to 37% of patients with congenital scoliosis^[52].

Congenital curves are typically inflexible and unresponsive to bracing^[53]. Surgical management is indicated for documented deformity progression, and for anomalies at high risk for progression. Published data have given some insight into the relative progression of commonly encountered malformations^[54]; however many of the deformities do not follow the simplified classification scheme, and serial radiographs are required during growth to understand and document progression. Additionally, the location of the vertebral anomaly also plays an important role in determining treatment. For example, small deformities at the lumbosacral or cervicothoracic junction can cause marked imbalance and large compensatory curves. Additionally the treatment of thoracic insufficiency syndrome, often seen in patients with multiple rib fusions or in patients with spondylocostal dysplasia, has recently been described as a surgical indication in patients with congenital vertebral

abnormalities to prevent cardiopulmonary comorbidities and allow for symmetric development of the chest and spine^[55,56].

Lumbosacral agenesis

Lumbosacral agenesis or caudal regression syndrome is a rare condition with an incidence of 1 in 25000 births. It is technically an anomaly of the caudal cell mass/filum terminale and is strongly associated with maternal hyperglycemia. Most commonly, this is seen in fetuses of mothers with preexisting uncontrolled diabetes (Figure 11) and is associated with vertebral, limb, genitourinary, and anal anomalies^[39].

Prenatal findings: Structurally, these patients have varying degrees of coccygeal, sacral, and lumbar agenesis with the abnormality beginning caudally and progressing cranially. The conus medullaris may have a truncated appearance in these patients both by MRI and ultrasound, and the diagnosis is usually first suspected when screening ultrasound demonstrates sacral agenesis. Recent literature suggests that conus morphology can also be evaluated in these patients prenatally with ultrasound utilizing high frequency linear transducers. Evaluation for Currarino triad is warranted in all patients with lumbosacral agenesis, which in addition to sacral anomalies, is comprised of anal atresia and a presacral mass (either teratoma or meningocele)^[16].

Postnatal evaluation and treatment: The clinical manifestations of sacral agenesis can vary depending on the extent of lumbosacral root involvement^[57]. Most patients have neuropathic bladder and are at increased risk for recurrent urinary tract infections and incontinence. Poor gastrointestinal motility and imperforate anus are also commonly seen. Neurologic involvement includes lower extremity muscle weakness and altered sensation^[58]. Equinovarus, lower extremity contractures, kyphoscoliosis and hypoplastic pelvis with

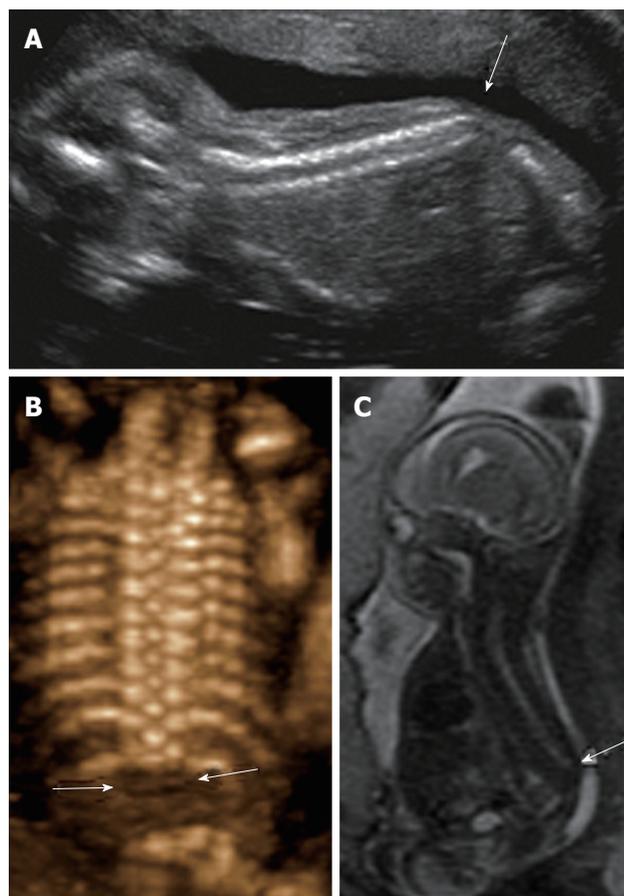


Figure 11 Sacral agenesis. 2D sagittal grayscale ultrasound (A), coronal 3D ultrasound (B), and parasagittal T1 weighted image (C) of a 19 wk fetus demonstrate absence of the fetal spine caudal to T12 (arrows), consistent with sacral agenesis/caudal regression syndrome. The mother was known to have type 1 diabetes, a risk factor for this condition.

hip instability are common orthopedic manifestations of this condition.

CONCLUSION

In summary, advances in prenatal ultrasonography and *in utero* MRI have given clinicians powerful tools to identify spinal pathologies during early stages of gestation. Prenatal counseling requires a “team” of appropriate specialists requiring coordination and cross-communication from multiple surgical and medical disciplines. The orthopedic clinician should critically assess the accuracy of the diagnosis, the likely natural history of the deformity, what treatments may be required, and what the impact of the anomaly will be on the child’s growth and eventual adult function.

REFERENCES

- 1 **Bernard JP**, Cuckle HS, Stirnemann JJ, Salomon LJ, Ville Y. Screening for fetal spina bifida by ultrasound examination in the first trimester of pregnancy using fetal biparietal diameter. *Am J Obstet Gynecol* 2012; **207**: 306.e1-306.e5 [PMID: 22683101 DOI: 10.1016/j.ajog.2012.05.014]

- 2 **Bulas D**. Fetal evaluation of spine dysraphism. *Pediatr Radiol* 2010; **40**: 1029-1037 [PMID: 20432022 DOI: 10.1007/s00247-010-1583-0]
- 3 **Simon EM**. MRI of the fetal spine. *Pediatr Radiol* 2004; **34**: 712-719 [PMID: 15316691 DOI: 10.1007/s00247-004-1245-1]
- 4 **Chao TT**, Dashe JS, Adams RC, Keefover-Hicks A, McIntire DD, Twickler DM. Fetal spine findings on MRI and associated outcomes in children with open neural tube defects. *AJR Am J Roentgenol* 2011; **197**: W956-W961 [PMID: 22021549 DOI: 10.2214/AJR.11.6745]
- 5 **Shekdar K**, Feygin T. Fetal neuroimaging. *Neuroimaging Clin N Am* 2011; **21**: 677-703, ix [PMID: 21807318 DOI: 10.1016/j.nic.2011.05.010]
- 6 **Azzoni R**, Gerevini S, Cabitza P. Spinal cord sonography in newborns: anatomy and diseases. *J Pediatr Orthop B* 2005; **14**: 185-188 [PMID: 15812289 DOI: 10.1097/01202412-200505000-00008]
- 7 **Pahys JM**, Samdani AF, Betz RR. Intraspinous anomalies in infantile idiopathic scoliosis: prevalence and role of magnetic resonance imaging. *Spine (Phila Pa 1976)* 2009; **34**: E434-E438 [PMID: 19454995 DOI: 10.1097/BRS.0b013e3181a2b49f]
- 8 **Rajasekaran S**, Kamath V, Kiran R, Shetty AP. Intraspinous anomalies in scoliosis: An MRI analysis of 177 consecutive scoliosis patients. *Indian J Orthop* 2010; **44**: 57-63 [PMID: 20165678 DOI: 10.4103/0019-5413.58607]
- 9 **Lowe LH**, Johaneck AJ, Moore CW. Sonography of the neonatal spine: part 1, Normal anatomy, imaging pitfalls, and variations that may simulate disorders. *AJR Am J Roentgenol* 2007; **188**: 733-738 [PMID: 17312061 DOI: 10.2214/AJR.05.2159]
- 10 **Khanna AJ**, Wasserman BA, Sponseller PD. Magnetic resonance imaging of the pediatric spine. *J Am Acad Orthop Surg* 2003; **11**: 248-259 [PMID: 12889863 DOI: 10.5435/00124635-200307000-00004]
- 11 **Olsen EA**, Brambrink AM. Anesthesia for the young child undergoing ambulatory procedures: current concerns regarding harm to the developing brain. *Curr Opin Anaesthesiol* 2013; **26**: 677-684 [PMID: 24184885 DOI: 10.1097/ACO.0000000000000016]
- 12 **Reddy SV**. Effect of general anesthetics on the developing brain. *J Anaesthesiol Clin Pharmacol* 2012; **28**: 6-10 [PMID: 22345937 DOI: 10.4103/0970-9185.92426]
- 13 **Abel TJ**, Chowdhary A, Gabikian P, Ellenbogen RG, Avellino AM. Acquired chiari malformation type I associated with a fatty terminal filum. Case report. *J Neurosurg* 2006; **105**: 329-332 [PMID: 17328286]
- 14 **Eule JM**, Erickson MA, O’Brien MF, Handler M. Chiari I malformation associated with syringomyelia and scoliosis: a twenty-year review of surgical and nonsurgical treatment in a pediatric population. *Spine (Phila Pa 1976)* 2002; **27**: 1451-1455 [PMID: 12131745 DOI: 10.1097/00007632-200207010-00015]
- 15 **Shaffer N**, Martin B, Loth F. Cerebrospinal fluid hydrodynamics in type I Chiari malformation. *Neurol Res* 2011; **33**: 247-260 [PMID: 21513645 DOI: 10.1179/01616411X12962202723805]
- 16 **Ben-Sira L**, Garel C, Malinger G, Constantini S. Prenatal diagnosis of spinal dysraphism. *Childs Nerv Syst* 2013; **29**: 1541-1552 [PMID: 24013324 DOI: 10.1007/s00381-013-2178-5]
- 17 **Blondiaux E**, Katorza E, Rosenblatt J, Nahama-Allouche C, Lenoir M, le Pointe HD, Garel C. Prenatal US evaluation of the spinal cord using high-frequency linear transducers. *Pediatr Radiol* 2011; **41**: 374-383 [PMID: 21221567 DOI: 10.1007/s00247-010-1922-1]
- 18 **Glenn OA**, Barkovich J. Magnetic resonance imaging of the fetal brain and spine: an increasingly important tool in prenatal diagnosis: part 2. *AJNR Am J Neuroradiol* 2006; **27**: 1807-1814 [PMID: 17032846]
- 19 **Warf BC**. Comparison of endoscopic third ventriculostomy alone and combined with choroid plexus cauterization in infants younger than 1 year of age: a prospective study in 550 African children. *J Neurosurg* 2005; **103**: 475-481 [PMID: 16383244 DOI: 10.3171/ped.2005.103.6.0475]
- 20 **Warf BC**, Campbell JW. Combined endoscopic third ventriculostomy and choroid plexus cauterization as primary treatment

- of hydrocephalus for infants with myelomeningocele: long-term results of a prospective intent-to-treat study in 115 East African infants. *J Neurosurg Pediatr* 2008; **2**: 310-316 [PMID: 18976099 DOI: 10.3171/PED.2008.2.11.310]
- 21 **Bowman RM**, Boshnjaku V, McLone DG. The changing incidence of myelomeningocele and its impact on pediatric neurosurgery: a review from the Children's Memorial Hospital. *Childs Nerv Syst* 2009; **25**: 801-806 [PMID: 19326126 DOI: 10.1007/s00381-009-0865-z]
 - 22 **Johnson CY**, Honein MA, Dana Flanders W, Howards PP, Oakley GP, Rasmussen SA. Pregnancy termination following prenatal diagnosis of anencephaly or spina bifida: a systematic review of the literature. *Birth Defects Res A Clin Mol Teratol* 2012; **94**: 857-863 [PMID: 23097374 DOI: 10.1002/bdra.23086]
 - 23 **Meuli M**, Moehrlen U. Fetal surgery for myelomeningocele: a critical appraisal. *Eur J Pediatr Surg* 2013; **23**: 103-109 [PMID: 23572465 DOI: 10.1055/s-0033-1343082]
 - 24 **Adzick NS**, Thom EA, Spong CY, Brock JW, Burrows PK, Johnson MP, Howell LJ, Farrell JA, Dabrowiak ME, Sutton LN, Gupta N, Tulipan NB, D'Alton ME, Farmer DL. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011; **364**: 993-1004 [PMID: 21306277 DOI: 10.1056/NEJMoa1014379]
 - 25 **Warf BC**. Hydrocephalus associated with neural tube defects: characteristics, management, and outcome in sub-Saharan Africa. *Childs Nerv Syst* 2011; **27**: 1589-1594 [PMID: 21928025 DOI: 10.1007/s00381-011-1484-z]
 - 26 **Sherk HH**, Uppal GS, Lane G, Melchionni J. Treatment versus non-treatment of hip dislocations in ambulatory patients with myelomeningocele. *Dev Med Child Neurol* 1991; **33**: 491-494 [PMID: 1864475 DOI: 10.1111/j.1469-8749.1991.tb14914.x]
 - 27 **Bemmerl JG**, Heimkes B. Neuromuscular function and radioanatomical form of the myelomeningocele hip. *J Pediatr Orthop B* 2000; **9**: 34-39 [PMID: 10647107 DOI: 10.1097/01202412-200001000-00007]
 - 28 **Drummond DS**, Moreau M, Cruess RL. The results and complications of surgery for the paralytic hip and spine in myelomeningocele. *J Bone Joint Surg Br* 1980; **62-B**: 49-53 [PMID: 7351435]
 - 29 **Leatherman KD**, Dickson RA. Congenital kyphosis in myelomeningocele. Vertebral body resection and posterior spine fusion. *Spine (Phila Pa 1976)* 1978; **3**: 222-226 [PMID: 715551 DOI: 10.1097/00007632-197809000-00006]
 - 30 **Micheli LJ**, Hall JE. The management of spine deformities in the myelomeningocele patient. *Med Ann Dist Columbia* 1974; **43**: 21-24 [PMID: 4590137]
 - 31 **Eyring EJ**, Wanken JJ, Sayers MP. Spine osteotomy for kyphosis in myelomeningocele. *Clin Orthop Relat Res* 1972; **88**: 24-30 [PMID: 4563943 DOI: 10.1097/00003086-197210000-00003]
 - 32 **Greene WB**. Treatment of hip and knee problems in myelomeningocele. *Instr Course Lect* 1999; **48**: 563-574 [PMID: 10098084]
 - 33 **Alman BA**, Bhandari M, Wright JG. Function of dislocated hips in children with lower level spina bifida. *J Bone Joint Surg Br* 1996; **78**: 294-298 [PMID: 8666645]
 - 34 **Thomson JD**, Ounpuu S, Davis RB, DeLuca PA. The effects of ankle-foot orthoses on the ankle and knee in persons with myelomeningocele: an evaluation using three-dimensional gait analysis. *J Pediatr Orthop* 1999; **19**: 27-33 [PMID: 9890282 DOI: 10.1097/00004694-199901000-00007]
 - 35 **Sharrard WJ**, Grosfield I. The management of deformity and paralysis of the foot in myelomeningocele. *J Bone Joint Surg Br* 1968; **50**: 456-465 [PMID: 4882210]
 - 36 **Warf BC**. Pathophysiology of tethered spinal cord, in *Pediatric Neurosurgery: Surgery of the Developing Nervous System*, 4th ed. In: McLone DG Editor. W.B. Saunders: Philadelphia, 2001: 282-288
 - 37 **Warf BC**. Tethered cord syndrome, in *Youman's Neurological Surgery*, 5th ed. In: Winn R Editor. W.B. Saunders: Philadelphia, 2004
 - 38 **Wolf S**, Schneble F, Tröger J. The conus medullaris: time of ascendance to normal level. *Pediatr Radiol* 1992; **22**: 590-592 [PMID: 1491937 DOI: 10.1007/BF02015359]
 - 39 **Lowe LH**, Johaneck AJ, Moore CW. Sonography of the neonatal spine: part 2, Spinal disorders. *AJR Am J Roentgenol* 2007; **188**: 739-744 [PMID: 17312062 DOI: 10.2214/AJR.05.2160]
 - 40 **Nejat F**, El Khashab M. Tethered cord. *J Neurosurg Pediatr* 2011; **7**: 681-682 [PMID: 21780321 DOI: 10.3171/2010.11.PEDS10403]
 - 41 **Sorantin E**, Robl T, Lindbichler F, Riccabona M. MRI of the neonatal and paediatric spine and spinal canal. *Eur J Radiol* 2008; **68**: 227-234 [PMID: 18762397 DOI: 10.1016/j.ejrad.2008.06.032]
 - 42 **Mete M**, Umur AS, Duransoy YK, Barutçuoğlu M, Umur N, Gurgun SG, Selçuki M. Congenital dermal sinus tract of the spine: experience of 16 patients. *J Child Neurol* 2014; **29**: 1277-1282 [PMID: 24563472 DOI: 10.1177/0883073813520501]
 - 43 **Kutuk MS**, Ozgun MT, Tas M, Poyrazoglu HG, Yikilmaz A. Prenatal diagnosis of split cord malformation by ultrasound and fetal magnetic resonance imaging: case report and review of the literature. *Childs Nerv Syst* 2012; **28**: 2169-2172 [PMID: 22940851 DOI: 10.1007/s00381-012-1900-z]
 - 44 **Pang D**, Dias MS, Ahab-Barmada M. Split cord malformation: Part I: A unified theory of embryogenesis for double spinal cord malformations. *Neurosurgery* 1992; **31**: 451-480 [PMID: 1407428 DOI: 10.1227/00006123-199209000-00010]
 - 45 **Cheng B**, Li FT, Lin L. Diastematomyelia: a retrospective review of 138 patients. *J Bone Joint Surg Br* 2012; **94**: 365-372 [PMID: 22371545 DOI: 10.1302/0301-620X.94B3.27897]
 - 46 **Goldstein I**, Makhoul IR, Weissman A, Drugan A. Hemivertebra: prenatal diagnosis, incidence and characteristics. *Fetal Diagn Ther* 2005; **20**: 121-126 [PMID: 15692206 DOI: 10.1159/000082435]
 - 47 **Tanaka T**, Uthoff HK. The pathogenesis of congenital vertebral malformations. A study based on observations made in 11 human embryos and fetuses. *Acta Orthop Scand* 1981; **52**: 413-425 [PMID: 6797230 DOI: 10.3109/17453678109050122]
 - 48 **Zelop CM**, Pretorius DH, Benacerraf BR. Fetal hemivertebrae: associated anomalies, significance, and outcome. *Obstet Gynecol* 1993; **81**: 412-416 [PMID: 8437797]
 - 49 **Varras M**, Akrivis C. Prenatal diagnosis of fetal hemivertebra at 20 weeks' gestation with literature review. *Int J Gen Med* 2010; **3**: 197-201 [PMID: 20689693]
 - 50 **Thawait GK**, Chhabra A, Carrino JA. Spine segmentation and enumeration and normal variants. *Radiol Clin North Am* 2012; **50**: 587-598 [PMID: 22643386 DOI: 10.1016/j.rcl.2012.04.003]
 - 51 **Unsinn KM**, Geley T, Freund MC, Gassner I. US of the spinal cord in newborns: spectrum of normal findings, variants, congenital anomalies, and acquired diseases. *Radiographics* 2000; **20**: 923-938 [PMID: 10903684 DOI: 10.1148/radiographics.20.4.g00j06923]
 - 52 **Basu PS**, Elsebaie H, Noordeen MH. Congenital spinal deformity: a comprehensive assessment at presentation. *Spine (Phila Pa 1976)* 2002; **27**: 2255-2259 [PMID: 12394903 DOI: 10.1097/00007632-200210150-00014]
 - 53 **Winter RB**. Spine deformity in children: Current concepts of diagnosis and treatment. *Pediatr Ann* 1976; **5**: 95-112 [PMID: 817255 DOI: 10.3928/0090-4481-19760401-10]
 - 54 **McMaster MJ**, Ohtsuka K. The natural history of congenital scoliosis. A study of two hundred and fifty-one patients. *J Bone Joint Surg Am* 1982; **64**: 1128-1147 [PMID: 7130226]
 - 55 **Campbell RM**, Smith MD, Mayes TC, Mangos JA, Willey-Courand DB, Kose N, Pinero RF, Alder ME, Duong HL, Surber JL. The effect of opening wedge thoracostomy on thoracic insufficiency syndrome associated with fused ribs and congenital scoliosis. *J Bone Joint Surg Am* 2004; **86-A**: 1659-1674 [PMID: 15292413]
 - 56 **Campbell RM**, Smith MD, Hell-Vocke AK. Expansion thoracoplasty: the surgical technique of opening-wedge thoracostomy. Surgical technique. *J Bone Joint Surg Am* 2004; **86-A** Suppl 1: 51-64 [PMID: 14996922]

- 57 **Pang D.** Sacral agenesis and caudal spinal cord malformations. *Neurosurgery* 1993; **32**: 755-778; discussion 778-779 [PMID: 8492851 DOI: 10.1097/00006123-199305000-00009]
- 58 **Emami-Naeini P,** Rahbar Z, Nejat F, Kajbafzadeh A, El Khashab

M. Neurological presentations, imaging, and associated anomalies in 50 patients with sacral agenesis. *Neurosurgery* 2010; **67**: 894-900; discussion 900 [PMID: 20881552 DOI: 10.1227/NEU.0b013e3181eb500d]

P- Reviewer: Singh K, Teli MGA, Zaminy A **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Wu HL



Basic Study

Evaluation of bone remodeling in regard to the age of scaphoid non-unions

Susanne Rein, Uwe Hanisch, Hans-Eberhard Schaller, Hans Zwipp, Stefan Rammelt, Stefan Weindel

Susanne Rein, Department of Plastic and Hand Surgery, Burn Unit, Trauma Center Bergmannstrost, 06112 Halle (Saale), Germany

Susanne Rein, Hans Zwipp, Stefan Rammelt, Center of Orthopaedics and Traumatology, University Medicine "Carl Gustav Carus" Dresden, Technical, University Dresden, 01307 Dresden, Germany

Uwe Hanisch, Institute of Pathology, "Carl Thiem" Hospital, 03048 Cottbus, Germany

Hans-Eberhard Schaller, Department of Plastic, Hand, Reconstructive and Burn Surgery, Trauma Center Tuebingen-University, 72076 Tuebingen, Germany

Stefan Weindel, Department of Hand, Aesthetic and Plastic Surgery, Hospital of Linth, 8730 Uznach, Switzerland

Author contributions: All authors made substantive intellectual contributions to this study, whether in the contributions to conception and design (Rein S, Hanisch U, Schaller HE, Zwipp H, Rammelt S, Weindel S), or acquisition of data (Rein S, Schaller HE, Weindel S), or analysis and interpretation of data (Rein S, Hanisch U, Schaller HE, Zwipp H, Rammelt S, Weindel S), or drafting and revising the manuscript critically (Rein S, Hanisch U, Schaller HE, Zwipp H, Rammelt S, Weindel S).

Institutional review board statement: This study was approved by the University of Tübingen Institutional review board (approval number: 367/2007A).

Informed consent statement: All patients gave their informed consent prior to surgery.

Conflict-of-interest statement: This study was financially supported by Zimmer Company, Münsingen, Switzerland. It is declared that the company was not involved in planning the experiment, and did not take part in data collection, analyses, interpretation of data or writing of the manuscript. The authors declare that they have no competing interests and disclose any financial conflicts of interest that may influence interpretation of this study and/or results.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Susanne Rein, MD, PhD, Department of Plastic and Hand Surgery, Burn Unit, Trauma Center Bergmannstrost, Merseburger Straße 165, 06112 Halle (Saale), Germany. susanne.rein@web.de

Telephone: +49-345-1326333

Fax: +49-345-1326334

Received: January 22, 2016

Peer-review started: January 22, 2016

First decision: March 1, 2016

Revised: March 26, 2016

Accepted: May 10, 2016

Article in press: May 11, 2016

Published online: July 18, 2016

Abstract

AIM: To analyse bone remodeling in regard to the age of scaphoid non-unions (SNU) with immunohistochemistry.

METHODS: Thirty-six patients with symptomatic SNU underwent surgery with resection of the pseudarthrosis. The resected material was evaluated histologically after staining with hematoxylin-eosin (HE), tartrate resistant acid phosphatase (TRAP), CD 68, osteocalcin (OC) and osteopontin (OP). Histological examination was performed in a blinded fashion.

RESULTS: The number of multinuclear osteoclasts in the TRAP-staining correlated with the age of the SNU and was significantly higher in younger SNU ($P = 0.034$; $r = 0.75$). A higher number of OP-immunoreactive osteoblasts significantly correlated with a higher number of OC-immunoreactive osteoblasts ($P = 0.001$; $r = 0.55$). Furthermore, a greater number of OP-immunoreactive osteoblasts correlated significantly with a higher number of OP-immunoreactive multinuclear osteoclasts ($P = 0.008$; $r = 0.43$). SNU older than 6 mo showed a significant decrease of the number of fibroblasts ($P = 0.04$). Smoking and the age of the patients had no influence on bone remodeling in SNU.

CONCLUSION: Multinuclear osteoclasts showed a significant decrease in relation to the age of SNU. However, most of the immunohistochemical findings of bone remodeling do not correlate with the age of the SNU. This indicates a permanent imbalance of bone formation and resorption as indicated by a concurrent increase in both osteoblast and osteoclast numbers. A clear histological differentiation into phases of bone remodeling in SNU is not possible.

Key words: Bone remodeling; Histology; Immunohistological staining; Scaphoid non-union; Scaphoid; Wrist joint

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The bone remodeling in regard to the age of scaphoid non-union is investigated with immunohistochemistry. Multinuclear osteoclasts showed a significant decrease in relation of the age of scaphoid non-union, but smoking and the age of the patients had no influence on bone remodeling. Most of the immunohistochemical findings of bone remodeling do not correlate with the age of the scaphoid non-unions, which indicates a permanent imbalance of bone formation and resorption.

Rein S, Hanisch U, Schaller HE, Zwipp H, Rammelt S, Weindel S. Evaluation of bone remodeling in regard to the age of scaphoid non-unions. *World J Orthop* 2016; 7(7): 418-425 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/418.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.418>

INTRODUCTION

The scaphoid is the most commonly fractured carpal bone^[1-3]. Scaphoid non-union (SNU) occurs in approximately 5% to 13% of treated scaphoid fractures and in an unknown number of unrecognized fractures^[2,4-6]. The reasons for this high non-union rate are multifactorial including fracture location and vascularity, failure of recognizing the fracture and inadequate initial treatment^[7,8]. Additionally, scaphoid fractures heal

by intramembranous ossification, which leaves the scaphoid without protective fracture callus against potentially disruptive forces. Progressive osteoarthritis, so called scaphoid non-union advanced collapse, inevitably develops in all cases with untreated SNU over time^[9].

Fracture healing consists of a regulatory circuit, which requires the proliferation and differentiation of osteoblasts and osteoclasts for bone regeneration and remodeling, together with formation of new blood vessels for bone vascularisation and a myriad of intercellular interactions and molecular communications to coordinate this complex process^[10]. Osteoblasts produce organic components of the extracellular matrix, regulate the mineralisation of the osteoid and therefore are essential for bone formation^[11,12]. Osteoclasts are responsible for bone resorption by removing mineralized matrix and breaking up the organic bone. Both osteoclasts and activated macrophages show a high expression of tartrate resistant acid phosphatase (TRAP) and glycoprotein CD 68. TRAP is synthesized as latent proenzyme and activated by proteolytic cleavage and reduction^[13,14]. Osteocalcin (OC) is an extracellular matrix protein produced by osteoblasts, which constitutes 2% of the total protein content in bone. It is distributed in cement lines of both cortical and trabecular bone^[15,16]. OC is thought to have a role in the early stages of bone healing and is a marker for bone formation^[17,18]. Osteopontin (OP) is a non-collagenous extracellular matrix protein and is biosynthesized by osteoblasts, osteoclasts, osteocytes, activated fibroblasts, hypertrophic chondrocytes and cemented lines^[16]. It is a multifunctional protein that is involved in several aspects of bone turnover and remodeling as well as fracture healing^[16,19].

A recent study found significant less bone remodeling in SNU older than a mean age of 45 mo^[20]. However, conventional histological investigation is not sufficient to analyze bone remodeling, because staining of the tissue is unspecific. Immunohistochemistry (IHC) using specific markers of bone resorption and bone formation is helpful to shed further light on the process of bone remodeling in SNU. It is hypothesized that there would be differences in numbers of immunohistochemically stained cells that would correlate with the age of the SNU. This difference in staining may lead to the identification of more bone formation (increase in osteoblasts) or bone resorption (increase in number of osteoclasts) over time and may generate more information about the development of SNU. Therefore the aim of this study was to evaluate bone remodeling of SNU with immunohistochemical markers in regard to the age of the fracture.

MATERIALS AND METHODS

Ethics

The study was conducted in accordance with the Helsinki Declaration. The local ethics committee review

board approved the study (367/2007A).

Patients

Thirty six male patients with a mean age of 26 (SD 12; range: 12-56) years at the time of injury were included in this study. Sixteen right and 20 left wrists were injured. The mean time between injury and surgery for non-union was 22 (SD 27; range: 4-144) mo. Six SNU were localised in the proximal third, 27 in the middle third, and one in the distal third of the scaphoid, respectively. In two patients, exact localisation of SNU was not defined. No additional surgery was performed during the follow-up period in 25 cases. However, one patient received a vascularised bone graft from the distal radius, one patient a four corner fusion, one patient a denervation of the wrist, and four patients another kind of wrist surgery in the postoperative follow-up. The data of the longer postoperative period in four patients were not available. Seventeen patients were non-smokers, 16 patients were smokers, but in three patients it was unclear, whether they are smokers or non-smokers.

Only patients, who stated a defined date of trauma having a symptomatic SNU, were included in this study. Exclusion criteria were unclear date of trauma, prior surgical treatment or associated adjacent injuries of the wrist as well as relevant underlying clinical diseases as diabetes mellitus or vascular disorders. Delayed fracture healing was defined between 4 to 6 mo. If no stable ossification was seen after 6 mo, the term non-union was used^[21].

Histological examination

During surgery the SNU was resected completely, whereas resection sides showed healthy bone verified by macroscopic bleeding. Autologous cancellous bone was interposed in the former SNU gap and compression osteosynthesis using a Herbert screw was performed^[22]. Specimens were immediately fixed in 4% neutral buffered (pH = 7.4) formaldehyde solution for 24 h at 4 °C, decalcified with diaminoethanetetraacetic acid and embedded in paraffin.

Sections of 2 µm were cut on a Leica rotation microtome (RM2055, Wetzlar, Germany) and mounted on silane-coated slides for conventional staining, enzyme- and IHC. HE-staining was performed in all specimens for morphological evaluation. Subsequently, the tissue sections were stained with TRAP, CD 68 (working dilution: 1:150, monoclonal, clone: KP-1, mouse anti-human, Dako, Glostrup, Denmark), OC (working dilution: 1:250, monoclonal, clone: OCG-3, mouse anti-human, Zytotec, Berlin, Germany) and OP (working dilution: 1:300, polyclonal, rabbit antisera, Chemicon, Temecula, Canada). Blocks and slides were stored at room temperature.

The mounted sections were dehydrated beginning with xylol in decreasing concentrations. Sections were then rehydrated with distilled water and pretreated according to the individual instructions from the suppliers of the used primary antibodies.

No special pretreatment was necessary for CD 68 and OC. For OP, specimens were treated with trypsin (pH = 6.0) for 30 min. After washing in phosphate-buffered saline solution (PBS, pH = 7.4), endogenous peroxidase activity was blocked in all sections with 1% hydrogen peroxide for 5 min. Nonspecific electrostatic protein charging was blocked with blocking reagent (Dako, Glostrup, Denmark) for 10 min at room temperature. Sections were incubated with respective normal sera (Linaris, Wertheim, Germany) for an hour at room temperature and then incubated overnight at 37 °C with primary antibodies. Biotinylated secondary antibodies were added for 30 min at 37 °C, followed by an avidin-biotin-enzyme complex for 30 min at 37 °C (Vectastain ABC-HRP kit, Linaris, PK-4000, Wertheim-Bettingen, Germany) at room temperature. The peroxidase activity was visualized with 3'-3'-diaminobenzidine. Then counterstaining with hematoxylin was performed. Sections were washed thoroughly three times in PBS for 5 min after each step. Finally, sections were dehydrated and covered with Entellan (Merck, Darmstadt, Germany). Control procedures, *i.e.*, identical staining without adding primary antibodies, were performed in parallel. Then counterstaining with hematoxylin was performed.

Histopathological examination of the stained tissue sections was performed using an Olympus BHS light microscope in the transmitted mode at final magnifications of 40 ×, 100 ×, 200 × and 400 ×. One section in each staining per subject was analysed. Total cell counts were counted at an original magnification of 100 × in 10 subsequent adjacent visual fields, representing the whole width of the non-union. Only fibroblasts were counted in 5 subsequent visual fields, because the volume of fibroblast tissue was not big enough for 10 visual fields in most cases. All specimens were blinded for cell counts.

Histopathological analysis was centered on osteopathological criteria including determination of chondrocytes and extracellular matrix (ECM) at the non-union gap, osteoblasts, osteoclasts, osteocytes, osteoid and cement lines of the underlying bone, mesenchymal cells and ECM in resorptive bone cysts as well as cysts containing fibrous or fibrocartilage tissue and typical hyaline cartilage in the OC and OP staining^[23].

Morphological analysis and cell counting

Morphological analysis was first performed with the HE-staining. With the help of the following criteria the different cell types were identified: Osteoblasts, which are mononuclear cells, were counted if they lined up the external surface of bone trabeculae and the surface of Haversian canals (Figure 1)^[23,24]. Osteocytes were counted if they were embedded into the mineralized bone matrix (Figure 1). Cells with two to fifteen nuclei in small resorptive excavations (Howship's lacunae) on the bone surface were counted as multinuclear osteoclasts (Figure 2).

Mononuclear osteoclast precursors could only be

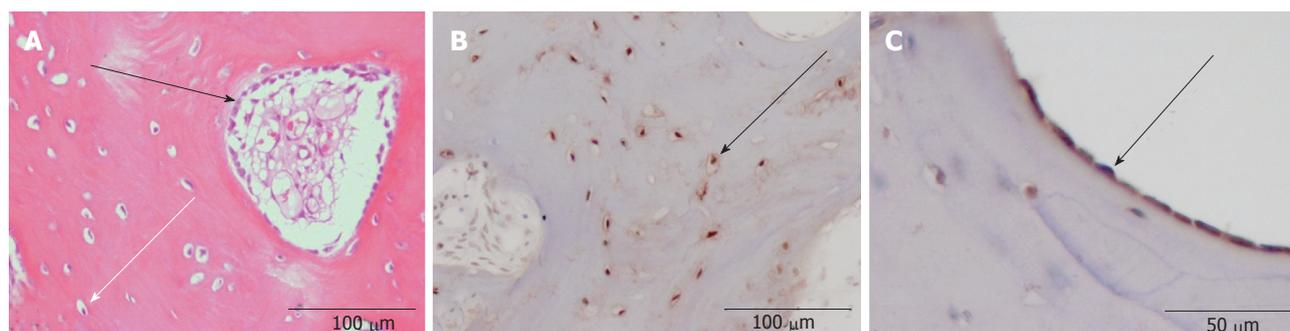


Figure 1 Morphological analysis. A 7-mo-old SNU is shown (A-C). A: HE-staining shows osteoblasts (black arrow) and osteocytes (white arrow) in the underlying sclerosed bone; B: OC-staining shows osteocytes (arrow) in detail; C: OP-staining shows the osteoblasts (arrow) lining a Haversian vessel in detail. Original magnification 200 × (A, B), 400 × (C). SNU: Scaphoid non-unions; OP: Osteopontin; OC: Osteocalcin.

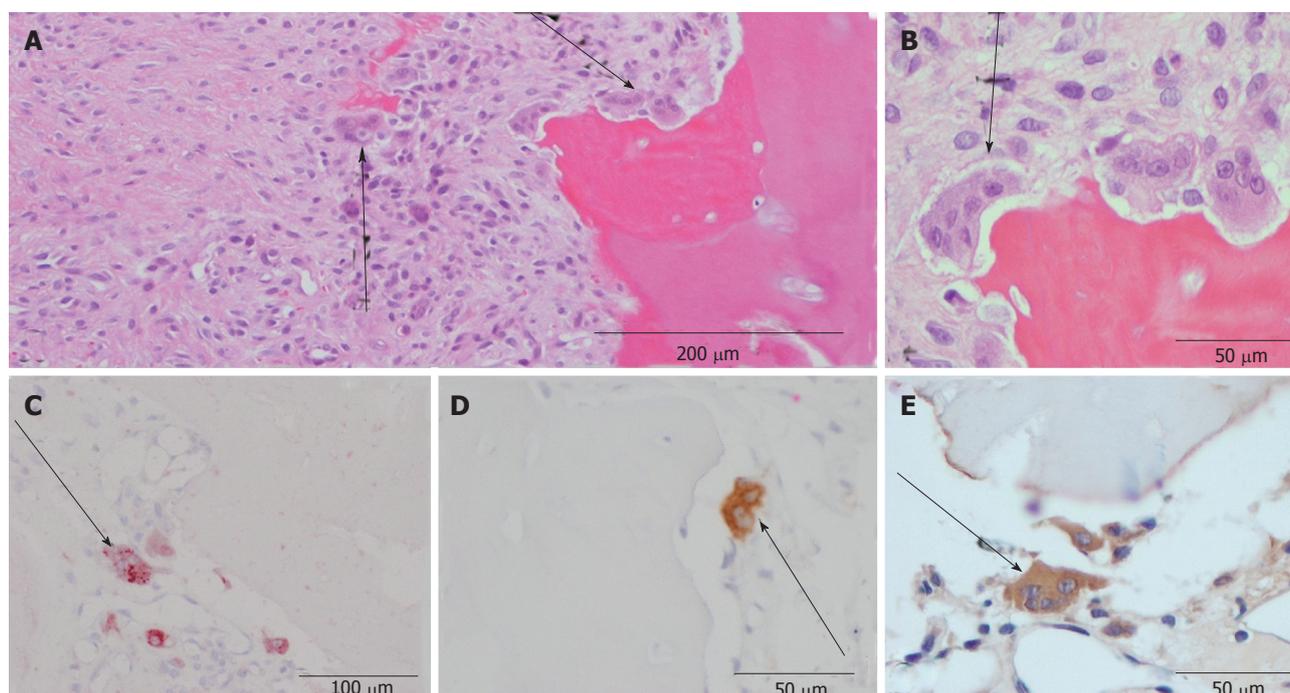


Figure 2 Osteoclasts. Examples for multinuclear osteoclasts as seen in the HE-staining (A and B), the TRAP (C), CD 68 (D) and OP (E) staining. (A-D) show osteoclasts (arrows) in a 10-mo-old SNU, whereas (E) shows an osteoclast in a 7-mo-old SNU. Original magnification 100 × (A), 200 × (C), 400 × (B, D, E). SNU: Scaphoid non-unions; OP: Osteopontin; TRAP: Tartrate resistant acid phosphatase.

identified in the TRAP and CD 68 staining and were counted as mononuclear positive-stained cells in these two stainings. Fibroblasts were counted as cells located in the non-union gap in the HE-staining (Figure 3).

Multinuclear osteoclasts were counted in the TRAP staining, with CD 68 and OP-IHC. Osteoblasts and osteocytes were counted with OP- and OC-IHC, respectively.

Data analysis

Statistical analysis was performed with a two sided *t* test in order to analyse the occurrence of OC- and OP-positive cells in the different parts of the SNU with a level of significance of $P \leq 0.05$.

The two-sided Pearson correlation analysis was used to investigate the linear relationship with regard to age of

SNU and patients, and counted cell numbers. Correlation analysis was performed with Spearman's rho coefficient with a significance level of $P \leq 0.05$. The influence of smoking has been investigated with the Kruskal-Wallis test followed by the Mann-Whitney test with a level of significance of $P \leq 0.05$. Statistical analysis was performed with the computer program SPSS (Version 11.5, Chicago, United States).

RESULTS

Immunohistochemical findings

Table 1 gives an overview over the markers that could reliably and reproducibly be detected. Negative procedures without antibodies showed no staining. OP was immunolocalized within chondrocytes and ECM

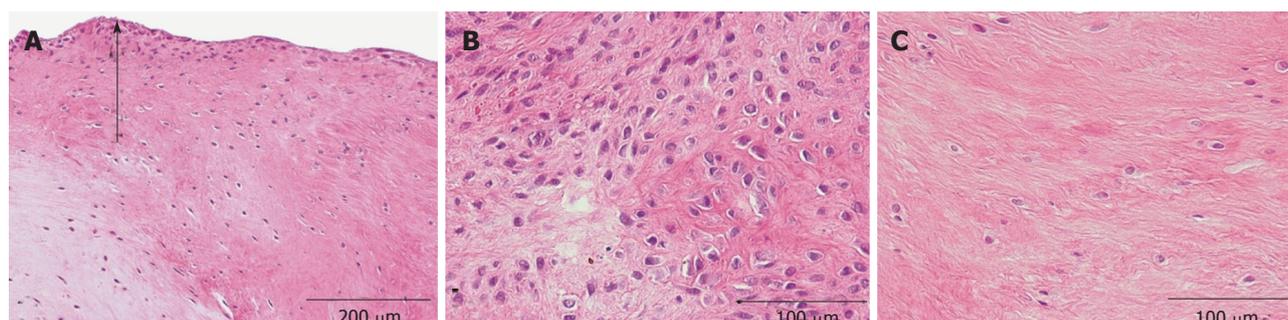


Figure 3 Non-union tissue in the hematoxylin-eosin staining. A: Non-union tissue with fibrocartilage covered by a layer of synovium-like lining cells (arrow) of a 60-mo-old SNU; B: Fibrous tissue rich in fibroblasts of a 10-mo-old SNU. Note the contrast in cell number as compared to the 60-mo-old SNU in A; C: Fibrous tissue with few fibroblasts, same patient as in A. Original magnification 100 × (A), 200 × (B, C). SNU: Scaphoid non-unions.

Table 1 Summary of the histological features with the range of time of their appearance

Histological feature		Immunohistochemical findings													
		Osteocalcin						OP							
		Yes (n)	Range of time (mo)		No (n)	Range of time (mo)		Not assessable (n)	Yes (n)	Range of time (mo)		No (n)	Range of time (mo)		Not assessable (n)
Non-union	Chondrocytes	1	12	12	35	4	144	-	25	4	144	11	6	60	-
	ECM	0	-	-	36	4	144	-	34	4	144	2	15	24	-
Underlying bone	Osteoblasts	31	6	144	4	4	22	1	34	4	144	2	9	15	-
	Osteoclasts	2	8	29	33	4	144	1	33	4	85	2	9	15	1
	Osteocytes	32	6	144	4	4	15	-	34	4	144	2	9	15	-
	Osteoid	13	7	28	23	4	144	-	32 ¹	4	85	4 ¹	14	144	-
	Cement lines	33	4	144	3	7	15	-	8	7	144	28	4	85	-
Resorptive bone cysts	Mesenchymal Cells	-	-	-	15	4	60	21	11	4	24	5	9	60	20
	ECM	-	-	-	15	4	60	21	15	4	60	1	15	15	20
Fibrous bone cysts	Mesenchymal cells	1	15	15	12	7	54	23	10	7	54	7	4	28	19
	ECM	1	15	15	12	7	54	23	12	7	54	5	4	24	19
Hyaline cartilage	Typical	33	4	144	2	9	12	1	34	4	144	1	15	15	1

The underlying bone's osteoid showed significantly more often OP-immunoreactivity in younger (18.5 ± 17.9 mo) than in older SNU (50.5 ± 62.7 mo) ($P = 0.02$). ECM: Extracellular matrix; OP: Osteopontin; SNU: Scaphoid non-unions.

of the non-union, osteoclasts, osteoblasts, osteoid and osteocytes of the underlying bone as well as the hyaline cartilage. Cement lines of newly formed lamellar bone only stained positively for OP in 8 out of 36 cases (Table 1). OC showed immunoreactivity in cement lines, osteocytes, osteoblasts and hyaline cartilage (Table 1). Resorptive and fibrous bone cysts showed immunoreactivity for OP in most cases but not for OC (Table 1). Enzyme-histochemical staining against TRAP specifically stained osteoclasts and mononuclear precursors indicating bone resorption during the remodeling process (Figure 2C). The macrophage marker CD 68 was detected in mononuclear and multinuclear macrophages or osteoclasts (Figure 2D). Mononuclear macrophages/osteoclast precursors and multinuclear osteoclasts stained positively for CD 68 in 32 out of 36 cases, whereas in only 8 out of 36 cases osteoclasts were stained positive for TRAP.

Osteoid showed immunoreactivity for OP in 32 younger SNU (18.5 SD 17.9 mo) with a range of age

between 4 to 85 mo, whereas there was no immunoreactivity for OP in 4 older SNUs (50.5 SD 62.7 mo) with a range of age between 14 to 144 mo. The difference between the two groups was statistical significant ($P = 0.02$; Table 1).

Cell counting and correlation analysis

Single results of the cell counting are presented in Table 2. The number of multinuclear osteoclasts in the TRAP-staining correlated with the age of the SNU and was significantly higher in younger SNU ($P = 0.034$; $r = 0.75$; Figure 4). All other correlations in regard to the age of the SNU showed no significant results.

A higher number of OP-immunoreactive osteoblasts significantly correlated with a higher number of OC-immunoreactive osteoblasts ($P = 0.001$; $r = 0.55$; Figure 5). Furthermore, a greater number of OP-immunoreactive osteoblasts correlated significantly with a higher number of OP-immunoreactive multinuclear osteoclasts ($P = 0.008$; $r = 0.43$; Figure 6).

Table 2 Results of the cell counting are shown as mean with standard deviation

Single results of the cell counting					
Histological feature	HE	TRAP (<i>n</i> = 8)	CD 68 (<i>n</i> = 32)	OP (<i>n</i> = 36)	OC (<i>n</i> = 36)
Osteoblasts	N/A	N/A	N/A	23.4 ± 12	25.6 ± 19.5
Osteoclasts					
Uninuclear	N/A	9 ± 6.5	4.6 ± 5.1	N/A	N/A
Multinuclear	N/A	2.3 ± 0.8	1.8 ± 1.2	1.1 ± 0.8	N/A
Osteocytes	N/A	N/A	N/A	38.2 ± 11.2	50.8 ± 16.4
Fibroblasts	285 ± 181	N/A	N/A	N/A	N/A

TRAP: Tartrate resistant acid phosphatase; CD 68: Cluster of differentiation 68; OC: Osteocalcin; OP: Osteopontin; N/A: Not analysed.

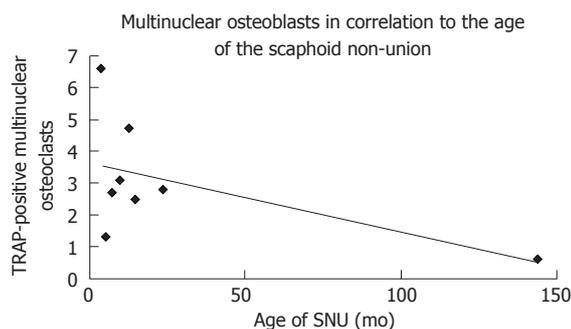


Figure 4 Multinuclear osteoclasts in correlation to the age of the scaphoid non-unions. The number of multinuclear osteoclasts in the TRAP-staining was significantly higher in younger SNU ($P = 0.034$; $r = 0.75$). SNU: Scaphoid non-unions; TRAP: Tartrate resistant acid phosphatase.

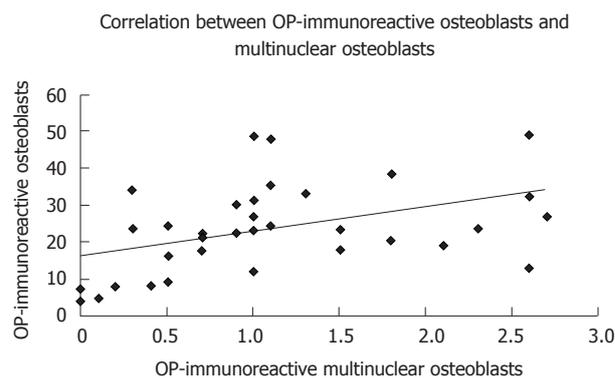


Figure 6 Correlation between osteopontin-immunoreactive osteoblasts and multinuclear osteoclasts. A greater number of OP-immunoreactive osteoblasts correlated significantly with a greater number of OP-immunoreactive multinuclear osteoclasts ($P = 0.008$; $r = 0.43$). OP: Osteopontin.

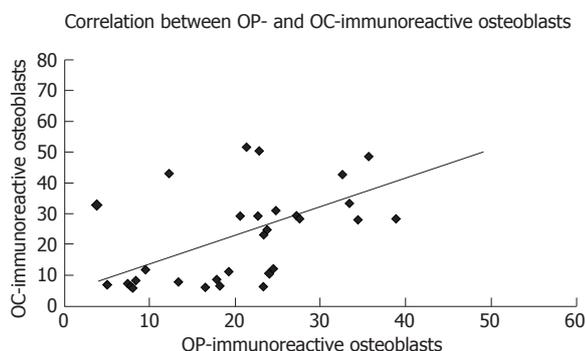


Figure 5 Correlation between osteoblasts in the osteopontin- and osteocalcin- immunohistochemistry. A greater number of OC-immunoreactive osteoblasts correlated significantly with a greater number of OP-immunoreactive osteoblasts ($P = 0.001$; $r = 0.55$). OC: Osteocalcin; OP: Osteopontin.

A mean of 285 (SD 181) fibroblasts were counted in the 36 investigated SNU in the HE staining. A mean of 457 (SD 175) fibroblasts were counted in SNU ($n = 4$) up to 6 mo old. In contrast, a mean of 264 (SD 173) fibroblasts were measured in SNU ($n = 32$) older than 6 mo. This was a significant decrease of fibroblasts in SNU, which are older than 6 mo ($P = 0.04$). However, no significant correlations have been found between the age of the patients and all investigated cell types. Furthermore, no significant differences have been observed between smokers and non-smokers for all investigated cell types.

DISCUSSION

A recent study has shown that significant less bone remodeling takes place in older SNU with a mean age of 45 mo compared to a mean age of 18 mo^[20]. However, these results were based on conventional HE-staining. Several bone-specific extracellular matrix proteins may be used to assess bone remodeling^[16]. OC is reportedly the most specific noncollagenous bone matrix protein, being expressed by osteoblasts and osteocytes^[25]. In the present study, we demonstrate specific staining of osteoblasts, osteocytes, cement lines, hyaline cartilage and in some cases osteoid ($n = 13$). OP is reportedly expressed by osteocytes, osteoblasts, and their precursors, osteoclasts, hypertrophic chondrocytes, and cement lines^[15,16]. We have seen specific staining of osteoblasts, osteoclasts, osteocytes, osteoid, chondrocytes, ECM of the non-union gap, and hyaline cartilage. OP interacts with osteoclasts, implicating it as a potentially important marker of bone resorption^[26].

A greater number of OC-immunoreactive osteoblasts correlated significantly with a greater number of OP-immunoreactive osteoblasts. However, correlation analysis between the two markers showed no time-dependent significant differences. Furthermore, a higher number of OP-immunoreactive osteoblasts correlated significantly with a higher number of OP-immunoreactive multinuclear osteoclasts, indicating a

higher bone remodeling in younger SNU. These findings confirm the theory that bone remodeling is a balance between bone formation and bone resorption in which osteoblasts exhibit two opposite phenotypes. There is the osteogenic phenotype, which secretes bone matrix at the bone resorption site, and the osteoclastogenic phenotype, which supports osteoclast differentiation in the old bone area^[11]. The close interplay between osteoblasts and osteoclasts during bone repair is well established^[10-12,17,23,24].

A recent study has shown that cell viability and mineralization-positive colony forming units were significantly reduced in osteoblasts retrieved from non-union sites. This study identified a set of significantly down-regulated factors in those "non-union osteoblasts" that are involved in the regulation of osteoblast proliferation and differentiation^[27]. This indicates that activity of osteoblasts in non-unions is altered, which could explain the lack of time-dependent changes in the OC- and OP-staining. However, another study could demonstrate, that OC-positive osteoblasts, which were taken from SNU, possessed osteogenic capability and could be stimulated by recombinant human bone morphogenetic protein-2 *in vitro*, resulting in significant increase in osteoblast differentiation and bone production^[28].

The number of osteoclasts decreased significantly in older SNU, which could be shown in the TRAP-staining, but not in the CD 68 IHC. This could be explained by the fact that CD 68 is not a specific osteoclast marker but rather a marker for several cells of the monocyte/macrophage lineage.

It is known, that nicotine has a dose dependent negative effect on bone healing, resulting in ischemia, diminished osteoblast function and decreased expression of bone morphogenetic protein^[29,30]. However, in this study nicotine abuse had no measurable influence on bone remodeling in SNU.

The high account of fibroblasts reflects a cell rich fibrous tissue in the non-union gap. We have seen a significant decrease of the count of fibroblasts in SNU older than 6 mo. Our explanation is that the instability in the non-union gap induces or provokes an activation of fibroblasts. For that reason, further research on this topic could be the investigation of proliferation with specific immunohistochemical markers, *e.g.*, Ki 67.

A greater number of OP-immunoreactive osteoblasts significantly correlated with a greater number of OC-immunoreactive osteoblasts and OP-immunoreactive multinuclear osteoclasts. Multinuclear osteoclasts show a significant decrease in older SNU. Fibroblasts showed a significant decrease in SNU, which are older than 6 mo. These results indicate a decreased bone remodeling in older SNU. On the other hand, permanent remodeling indicates mechanical instability and imbalance. Therefore most of the immunohistochemical markers of bone remodeling do not correlate with the age of the SNU. Smoking had no influence on bone remodelling in SNU.

ACKNOWLEDGMENTS

The authors thank Ursula Range for her advice with the statistical analysis, Suzanne Manthey and Doreen Küchler for histological preparation as well as Thomas Albrecht for preparation of the photographs.

COMMENTS

Background

The scaphoid is the most commonly fractured carpal bone, whereas non-union occurs in approximately 5% to 13% of treated scaphoid fractures.

Research frontiers

Conventional histological stainings are insufficient to analyze bone remodeling, because staining of the tissue is unspecific.

Innovations and breakthroughs

Immunohistochemistry using specific markers of bone resorption and bone formation is helpful to shed further light on the process of bone remodeling in scaphoid non-union.

Applications

Multinuclear osteoclasts, as a marker for bone resorption, showed a significant decrease in relation of the age of scaphoid non-union, but smoking and the age of the patients had no influence on bone remodeling. Most of the immunohistochemical findings of bone remodeling do not correlate with the age of the scaphoid non-unions (SNU), which indicates a permanent imbalance of bone formation and resorption.

Peer-review

This is a study on the bone remodeling in regard to the age of SNU with immunohistochemistry. The rationale for the study is appropriate and it is an interesting paper with a valuable contribution.

REFERENCES

- 1 **Dunn AW.** Fractures and dislocations of the carpus. *Surg Clin North Am* 1972; **52**: 1513-1538 [PMID: 4564432]
- 2 **Leslie IJ, Dickson RA.** The fractured carpal scaphoid. Natural history and factors influencing outcome. *J Bone Joint Surg Br* 1981; **63-B**: 225-230 [PMID: 7217146]
- 3 **Hove LM.** Epidemiology of scaphoid fractures in Bergen, Norway. *Scand J Plast Reconstr Surg Hand Surg* 1999; **33**: 423-426 [PMID: 10614752 DOI: 10.1080/02844319950159145]
- 4 **Düppe H, Johnell O, Lundborg G, Karlsson M, Redlund-Johnell I.** Long-term results of fracture of the scaphoid. A follow-up study of more than thirty years. *J Bone Joint Surg Am* 1994; **76**: 249-252 [PMID: 8113260]
- 5 **Eddeland A, Eiken O, Hellgren E, Ohlsson NM.** Fractures of the scaphoid. *Scand J Plast Reconstr Surg* 1975; **9**: 234-239 [PMID: 1219995 DOI: 10.3109/02844317509022872]
- 6 **Dias JJ, Brenkel IJ, Finlay DB.** Patterns of union in fractures of the waist of the scaphoid. *J Bone Joint Surg Br* 1989; **71**: 307-310 [PMID: 2925752]
- 7 **Perlik PC, Guilford WB.** Magnetic resonance imaging to assess vascularity of scaphoid nonunions. *J Hand Surg Am* 1991; **16**: 479-484 [PMID: 1861031 DOI: 10.1016/0363-5023(91)90018-7]
- 8 **Pandit S, Wen DY.** Scaphoid fractures with unusual presentations: a case series. *Cases J* 2009; **2**: 7220 [PMID: 19829935 DOI: 10.4076/1757-1626-2-7220]
- 9 **Lindström G, Nyström A.** Natural history of scaphoid non-union, with special reference to "asymptomatic" cases. *J Hand Surg Br* 1992; **17**: 697-700 [PMID: 1484258 DOI: 10.1016/0266-7681(92)90204-F]
- 10 **Schweiberer L, Baumgart R, Deiler S.** The biological reaction in

- atrophic and hypertrophic pseudarthrosis of diaphysis of long bone. Causes and forms of appearance. *Chirurg* 1999; **70**: 1193-1201 [PMID: 10591755 DOI: 10.1007/s001040050770]
- 11 **Nakahama K.** Cellular communications in bone homeostasis and repair. *Cell Mol Life Sci* 2010; **67**: 4001-4009 [PMID: 20694737 DOI: 10.1007/s00018-010-0479-3]
 - 12 **Owen M.** Lineage of osteogenic cells and their relationship to the stromal system. In: *Bone and Mineral Research*. 1985: 1-25
 - 13 **Ljusberg J, Ek-Rylander B, Andersson G.** Tartrate-resistant purple acid phosphatase is synthesized as a latent proenzyme and activated by cysteine proteinases. *Biochem J* 1999; **343** Pt 1: 63-69 [PMID: 10493912 DOI: 10.1042/0264-6021]
 - 14 **Ljusberg J, Wang Y, Lång P, Norgård M, Dodds R, Hulthenby K, Ek-Rylander B, Andersson G.** Proteolytic excision of a repressive loop domain in tartrate-resistant acid phosphatase by cathepsin K in osteoclasts. *J Biol Chem* 2005; **280**: 28370-28381 [PMID: 15929988 DOI: 10.1074/jbc.M502469200]
 - 15 **Ingram RT, Clarke BL, Fisher LW, Fitzpatrick LA.** Distribution of noncollagenous proteins in the matrix of adult human bone: evidence of anatomic and functional heterogeneity. *J Bone Miner Res* 1993; **8**: 1019-1029 [PMID: 8237471 DOI: 10.1002/jbmr.5650080902]
 - 16 **Rammelt S, Corbeil D, Manthey S, Zwipp H, Hanisch U.** Immunohistochemical in situ characterization of orthopedic implants on polymethyl metacrylate embedded cutting and grinding sections. *J Biomed Mater Res A* 2007; **83**: 313-322 [PMID: 17437302 DOI: 10.1002/jbm.a.31243]
 - 17 **Rammelt S, Neumann M, Hanisch U, Reinstorf A, Pompe W, Zwipp H, Biewener A.** Osteocalcin enhances bone remodeling around hydroxyapatite/collagen composites. *J Biomed Mater Res A* 2005; **73**: 284-294 [PMID: 15800855 DOI: 10.1002/jbm.a.30263]
 - 18 **Hauschka PV, Lian JB, Cole DE, Gundberg CM.** Osteocalcin and matrix Gla protein: vitamin K-dependent proteins in bone. *Physiol Rev* 1989; **69**: 990-1047 [PMID: 2664828]
 - 19 **Yamazaki M, Nakajima F, Ogasawara A, Moriya H, Majeska RJ, Einhorn TA.** Spatial and temporal distribution of CD44 and osteopontin in fracture callus. *J Bone Joint Surg Br* 1999; **81**: 508-515 [PMID: 10872376 DOI: 10.1302/0301-620X.81B3.9398]
 - 20 **Rein S, Hanisch U, Rammelt S, Schmidt G, Schaller HE, Zwipp H, Oehmke M, Weindel S.** Histopathological, radiological and clinical aspects of the temporal assignment of scaphoid non-union. *Arch Orthop Trauma Surg* 2010; **130**: 1243-1250 [PMID: 19949806 DOI: 10.1007/s00402-009-1010-x]
 - 21 **Rüter A, Mayr E.** Pseudarthrosis. *Chirurg* 1999; **70**: 1239-1245 [PMID: 10591760 DOI: 10.1007/s001040050775]
 - 22 **Herbert TJ, Fisher WE.** Management of the fractured scaphoid using a new bone screw. *J Bone Joint Surg Br* 1984; **66**: 114-123 [PMID: 6693468]
 - 23 **Athanasou N.** Injury and repair of skeletal tissues. In: *Pathological basis fo orthopaedic and rheumatic disease. Clinical, radiological, and pathological correlation of diseases of bone, joint, and soft tissue*. Hodder Arnold: Gran Bretagna, 2001
 - 24 **Lian J, Stein G, Canalis E.** Bone formation: osteoblast lineage cells, growth factors, matrix proteins and the mineralization process. Philadelphia: Lippincott-Williams & Wilkins, 1999
 - 25 **Kato Y, Windle JJ, Koop BA, Mundy GR, Bonewald LF.** Establishment of an osteocyte-like cell line, MLO-Y4. *J Bone Miner Res* 1997; **12**: 2014-2023 [PMID: 9421234 DOI: 10.1359/jbmr.1997.12.12.2014]
 - 26 **Miyauchi A, Alvarez J, Greenfield EM, Teti A, Grano M, Colucci S, Zamboni-Zallone A, Ross FP, Teitelbaum SL, Cheresch D.** Recognition of osteopontin and related peptides by an alpha v beta 3 integrin stimulates immediate cell signals in osteoclasts. *J Biol Chem* 1991; **266**: 20369-20374 [PMID: 1939092]
 - 27 **Hofmann A, Ritz U, Hessmann MH, Schmid C, Tresch A, Rompe JD, Meurer A, Rommens PM.** Cell viability, osteoblast differentiation, and gene expression are altered in human osteoblasts from hypertrophic fracture non-unions. *Bone* 2008; **42**: 894-906 [PMID: 18314404 DOI: 10.1016/j.bone.2008.01.013]
 - 28 **Qu G, von Schroeder HP.** The osteogenic potential of pseudoarthrosis tissue and bone from human scaphoid non-unions. *J Hand Surg Eur Vol* 2008; **33**: 449-456 [PMID: 18579620 DOI: 10.1177/1753193408090122]
 - 29 **Hollinger JO, Schmitt JM, Hwang K, Soleymani P, Buck D.** Impact of nicotine on bone healing. *J Biomed Mater Res* 1999; **45**: 294-301 [PMID: 10321701 DOI: 10.1002/(SICI)1097-4636(19990615)45]
 - 30 **Ma L, Zheng LW, Cheung LK.** Influence of nicotine on blood perfusion and bone healing during distraction osteogenesis. *Ann R Australas Coll Dent Surg* 2008; **19**: 52-54 [PMID: 19728631]

P- Reviewer: Luo XH, Maia LP S- Editor: Qiu S L- Editor: A
E- Editor: Wu HL



Case Control Study

Computerized tomography based "patient specific blocks" improve postoperative mechanical alignment in primary total knee arthroplasty

Raju Vaishya, Vipul Vijay, Vikas P Birla, Amit K Agarwal

Raju Vaishya, Vipul Vijay, Vikas P Birla, Amit K Agarwal, Department of Orthopaedics, Joint Replacement and Arthroscopy, Indraprastha Apollo Hospital, New Delhi 110076, India

Author contributions: Vaishya R helped in performing the surgery and designing the research; Vijay V helped in data collection and preparation of the manuscript; Birla VP helped in data collection and statistics; Agarwal AK helped in preparation of manuscript.

Institutional review board statement: The study was approved by the IRB of the institution.

Informed consent statement: All the patients included in the study gave an informed consent for inclusion in the study.

Conflict-of-interest statement: No conflicts of interest to declare.

Data sharing statement: The authors are willing to share the data of the present study.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Vipul Vijay, Department of Orthopaedics, Joint Replacement and Arthroscopy, Indraprastha Apollo Hospital, Sarita Vihar, New Delhi 110076, India. dr_vipulvijay@yahoo.com
Telephone: +91-11-29871210

Received: January 11, 2016

Peer-review started: January 14, 2016

First decision: February 29, 2016

Revised: March 14, 2016

Accepted: May 7, 2016

Article in press: May 9, 2016

Published online: July 18, 2016

Abstract

AIM: To compare the postoperative mechanical alignment achieved after total knee arthroplasty (TKA) using computer tomography (CT) based patient specific blocks (PSB) to conventional instruments (CI).

METHODS: Total 80 knees were included in the study, with 40 knees in both the groups operated using PSB and CI. All the knees were performed by a single surgeon using the same cruciate sacrificing implants. In our study we used CT based PSB to compare with CI. Postoperative mechanical femoro-tibial angle (MFT angle) was measured on long leg x-rays using picture archiving and communication system (PACS). We compared mechanical alignment achieved using PSB and CI in TKA using statistical analysis.

RESULTS: The PSB group (group 1) included 17 females and seven males while in CI group (group 2) there were 15 females and eight males. The mean age of patients in group 1 was 60.5 years and in group 2 it was 60.2 years. The mean postoperative MFT angle measured on long-leg radiographs in group 1 was 178.23° (SD = 2.67°, range: 171.9° to 182.5°) while in group 2, the mean MFT angle was 175.73° (SD = 3.62°, range: 166.0° to 179.8°). There was significant improvement in postoperative mechanical alignment (P value = 0.001), in PSB group compared to CI. Number of outliers were also found to be less in group operated with PSB (7 Knee) compared to those operated with CI (17 Knee).

CONCLUSION: PSB improve mechanical alignment after total knee arthroplasty, compared to CI. This may lead to lower rates of revision in the PSB based TKA as compared to the conventional instrumentation.

Key words: Knee; Replacement; Arthroplasty; Patient specific jigs; Conventional jigs

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Computer tomography (CT) based patient specific blocks (PSB) can help restore the mechanical axis of the patients undergoing primary total knee replacement. In the present study, the PSB group had significantly better post-operative mechanical axis as compared to the conventional instrumentation group. CT based PSB holds promise to help in accurate restoration of the mechanical axis and might decrease the rates of revision after total knee arthroplasty.

Vaishya R, Vijay V, Birla VP, Agarwal AK. Computerized tomography based “patient specific blocks” improve postoperative mechanical alignment in primary total knee arthroplasty. *World J Orthop* 2016; 7(7): 426-433 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/426.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.426>

INTRODUCTION

Total knee arthroplasty (TKA) has been a successful surgery providing excellent functional results in a patient with an advanced degenerative joint disease of the knee. It has been accepted that postoperative lower limb alignment is an important parameter for favorable functional outcomes in TKA^[1]. Arthroplasty surgeons aim to achieve an average mechanical angle (*i.e.*, 180°) and any variation more than 3° may lead to poor functional results and early implant failure^[2,3]. Therefore, postoperative mechanical alignment has been considered an important index for a successful surgery amongst arthroplasty surgeons.

The commonly used conventional instruments (CI) in TKA consist of intramedullary (I/M) femoral alignment guide and extramedullary (E/M) tibial alignment guide. Although these instruments are familiar to most surgeons and easy to use, they have demonstrated a limited degree of accuracy^[4]. The CI used as I/M femoral guide is aligned on the basis of anatomical axis of the femur. However, the surgeon intends to have distal femur bone cut perpendicular to the mechanical axis (MA) of the femur. In this technique, the surgeon has to make an assumption about the femoral valgus angle which may lead to error in bone cuts, due to the discrepancy in the assumed and the real femoral valgus angle. Also, there could be errors in rotational alignment that is estimated using the epicondylar axis or the anteroposterior axis as popularized by Whiteside

et al^[5]. The epicondylar axis is hard to determine and can lead to significant inter as well as intra-observer variability^[6-8]. The I/M guide is dependent on an exact fit of the rod in the femoral canal, which is not always obtained and on the position of the entrance hole in the femur, which is user dependent and may significantly alter the distal femoral mechanical angle^[9-12]. Due to several inherent limitations of CI, there was a need for improvement, and this has prompted efforts to develop a more precise surgical technology for restoring an accurate mechanical axis after TKA.

This initiative led the development of computer-assisted surgery (CAS) techniques. Although, CAS has been shown to improve MA over CI, it is also associated with disadvantages like increased surgical time, expensive instrumentation, steep learning curve, higher number of personnel required and higher infection rates^[13,14].

Patient specific blocks (PSB) were introduced as an alternative to CAS and CI, with the goal of improving postoperative alignment, implant positioning and overcoming the shortcomings associated with the CAS and CI. These blocks were manufactured before the surgery after a computerized tomography (CT) analysis (Figure 1). The primary aim of these blocks is to optimize the bone cuts so as to achieve accurate MA of the lower limb. There has been recent interest seen in the literature regarding the use and efficacy of patient specific instruments (PSI) in achieving the optimal MA after TKA. But, until now the published reports comparing PSI and CI in primary TKA vary regarding the actual advantages of PSB^[15-19].

We undertook this study with the aim to compare the postoperative mechanical alignment achieved using PSI and CI in TKA to assess the efficacy of CT-based PSB in the achievement of anatomical alignment after primary TKA.

MATERIALS AND METHODS

This study was a prospective, comparative single study conducted over a period of one year. All the patients who came with severe degenerative arthritis of knee (Ahlback's grade 3 or 4) and planned for TKA during the period from November 2013 to October 2014 in one unit were included in this study. An approval from the institutional review board was taken. As the technique of PSB was still new and very few patients were aware of it, all the subjects were first explained and made familiar with the technique of PSB and its difference from CI for TKA. Patient were informed about the expected benefits and advantages of PSB, and also about the extra cost of 400\$ per knee involved in using the PSB (cost of CT Scannogram and manufacturing of the blocks). Subjects who were ready to bear the extra cost, willing to undergo the CT scan, and gave consent were operated using PSB, and were named as group 1. Remaining subjects were conducted using CI and designated as group 2.

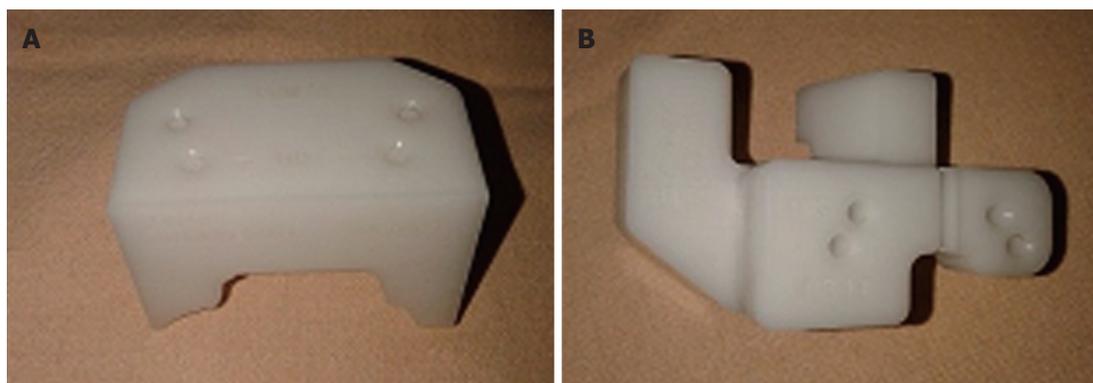


Figure 1 Patient specific blocks used in the present study (A: Femoral jig, B: Tibial jig).



Figure 2 Tibial jig conforming to the proximal tibial anatomy and fitting well to the bone. This jig is used for insertion of the proximal tibial pins followed by use of the conventional proximal tibial jig.



Figure 3 Femoral jig matching the contour of the anterior femoral cortex.

Each group included 40 knees. Most of the knees had varus deformity except six knees in each group having a valgus deformity. CT scan of group 1 subjects was done preoperatively in the same institute and data sent to PSB manufacturing unit. PSB manufactured from Stryker® was used for all subjects in group 1 (Figure 1). Stryker Scorpio™ posterior stabilized knee system was used in all the patients.

An anterior-posterior radiograph of the knee in standing and lateral positions was done preoperatively. Each of these patients was operated by the same surgeon (RV) in the same operating setup and using a similar protocol.

An anterior midline longitudinal incision with modified Insall's approach^[20] was used in all the TKA and the majority of operating steps were same in both the groups, except that the alignment guides (PSB) were used in group 1 (Figures 2 and 3). In group 2, E/M alignment guide for tibia and I/M alignment guide for femur were used. The tibial alignment guide was adjusted to achieve 0° varus/valgus cut with 5° posterior slope, whereas on the femoral side 50 valgus (which was reduced to 30 valgus for valgus knees) and 30 external rotation was kept in the alignment guide. The decision to change the femoral valgus angle in the valgus knees in the CI group was taken based on standard protocol and was not based on any pre-

operative femoral valgus angle calculation.

We aimed to achieve a rectangular gap of 20 mm which was equally symmetrical in both flexion and extension. All the modifications required in operating steps for proper bone cuts to achieve accurate alignment were done intraoperatively in group 2 patients performed with CI. Whereas, in group 1 patients all the planning was done preoperatively, which started with preoperative CT scannogram followed by an assessment of bone cut on virtual bone models and finally fabrication of blocks after approval from the operating surgeon (Figure 1). These blocks were then used intraoperatively to decide the pin position over which a conventional cutting jig was placed for planned bone cuts.

The primary aim of this study was to compare the postoperative mechanical alignment achieved with using PSI and CI in TKA. The MA was assessed by measuring the Mechanical femoral-tibial angle (MFT angle) on a long-leg radiograph of lower limb done on second follow-up visits, planned after one month of surgery, as most of the patients were able to stand erect with full knee extension and without any support (Figure 4). All the MFT angles were measured by a single individual of the operating unit (VB) who first underwent adequate training in the measurement of the MFT angle on long leg standing radiographs. Outliers of the mechanical axis after total knee arthroplasty were defined as those patients who had values of mechanical axis ± 3 degrees

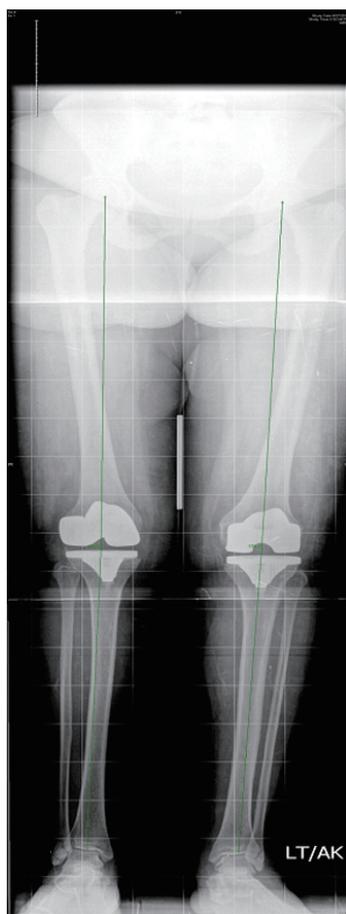


Figure 4 Postoperative weight bearing long leg radiograph measuring the hip-knee-ankle axis (mechanical axis).

from the neutral 180°. Thus, inter-observer and intra-observer variation were avoided. Data from both the groups was analyzed and compared using statistical analysis as mentioned below.

Statistical analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables were presented as mean \pm SD or median and categorical variables were presented as absolute numbers and percentage. Data were checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired *t* test, whereas the Mann-Whitney *U* test was used for those variables that were not normally distributed. Categorical variables were analyzed using either the χ^2 test or Fisher's exact test. For all statistical tests, a *P* value less than 0.05 were taken to indicate a significant difference.

RESULTS

The study group 1 included 17 females and seven males while in group 2 there were 15 females and eight males. The mean age of patients in group 1 was 60.5 years and in group 2 it was 60.2 years. In group 1, 16 patients had bilateral, and 8 had unilateral

Table 1 comparison of post-operative mechanical femoral tibial angle between the patient specific block group and the conventional group

	PSB group (<i>n</i> = 40) Mean \pm SD	Conventional group (<i>n</i> = 40) Mean \pm SD	Mean difference	<i>P</i> value
Postop MFT angle	178.23 \pm 2.67	175.73 \pm 3.62	2.497	0.001

Postop: Post operation; MFT: Mechanical femoro-tibial; PSB: Patient specific blocks.

TKA. In group 2, 17 patients had bilateral, and 6 had unilateral TKA. No significant difference was found between the two groups concerning age, sex, and sidewise distribution. The mean postoperative MFT angle measured on long-leg radiographs in group 1 was 178.23° (SD = 2.67°, range - 171.9° to 182.5°) while in group 2, the mean MFT angle was 175.73° (SD = 3.62°, range - 166.0° to 179.8°) (Table 1). There was a significant difference in postoperative MA achieved in PSI (group 1) compared to CI (group 2) with *p*-value = 0.001. In group 1 there were 7 outliers while in group 2, there were 17 outliers (Figures 5 and 6). Thus, there was also increase in outliers in group 2 compared to group 1. There was a significant difference in outliers achieved in PSI (group 1) compared to CI (group 2) with *p*-value = 0.0147 (Figures 5 and 6).

DISCUSSION

The number of TKA annually is increasing every year, but the main concern for a surgeon and patient undergoing primary TKA remains long-term survival of the implant. Also, the increased morbidity, healthcare cost and complications associated with revision surgery have further guided the arthroplasty surgeons to strive for longer implant survival. One of the most important factors contributing to implant survival is accurate mechanical alignment. Various techniques like computer navigation, PSI, *etc.*, have been introduced to achieve precise mechanical alignment in TKA.

The importance of accurate postoperative mechanical alignment of lower limb for the successful outcome of TKA has been accepted widely and supported by several studies. As early as in 1977, Lotke *et al.*^[21] reported the importance of accurate implant positioning in the long term survival of knee implants. These findings were further corroborated by Ritter *et al.*^[2] who demonstrated an increased failure rate for knees in varus. Sharkey *et al.*^[3] concluded that most of the revisions which were performed within the first two years of primary surgery were due to errors in surgical technique. This background knowledge prompted the development and introduction of PSI with the aim of improving post-operative mechanical alignment while bypassing the drawbacks of CAS. Improvement in mechanical alignment with the use of PSI in TKA was first reported

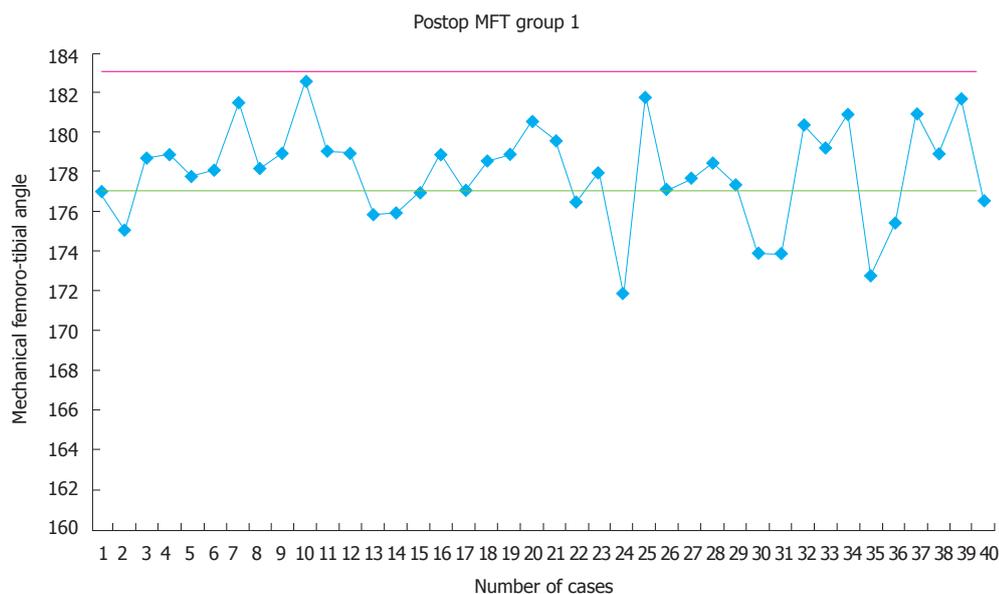


Figure 5 Scatter diagram depicting the distribution of the post-operative mechanical femoro-tibial angle (mechanical femoro-tibial angle) in the patient specific block group (group 1). MFT: Mechanical femoro-tibial angle.

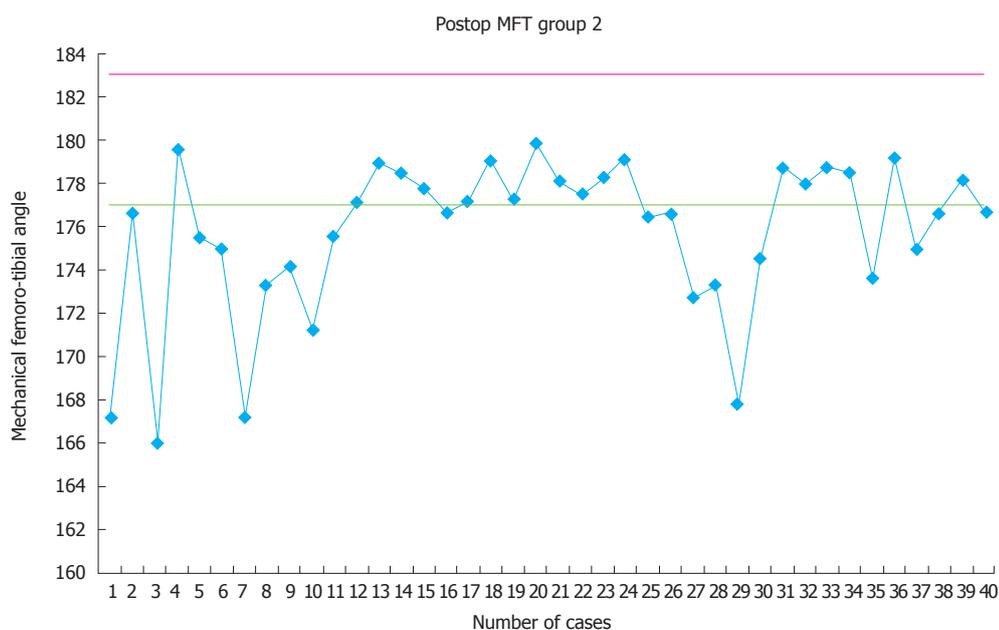


Figure 6 Scatter diagram depicting the distribution of the post-operative mechanical femoro-tibial angle (mechanical femoro-tibial angle) in the conventional instrument group (group 2). MFT: Mechanical femoro-tibial angle.

by Hafez *et al*^[22] on cadaveric knees and plastic bones. Similar results were obtained from a study done by Ng *et al*^[4] where they compared 569 TKA done with PSI to 155 TKA done with conventional instruments and found decreased a number of outliers with PSI. The numbers of outliers with any technique used in TKA remains an important observation and indicate the efficacy of that technique. We also found decreased outliers with the use of PSI, in our study. Heyse *et al*^[23] and Renson *et al*^[24] also noticed decreased the number of outliers with PSI (13%) compared to conventional jig (29%).

However, some authors found contradictory results

in their studies. Abane *et al*^[25] compared 70 TKA done with PSI to an equal number of TKA done with CI and could not find any significant improvement in the post operative MA with the use PSI over CI. Klatt *et al*^[26] reported 4 patients operated with PSI showed malalignment in mechanical axis. From their small case series, they opined that this emerging technology ignores conventional principles of TKA and the software used unreliable at present. Chen *et al*^[16] in their study of 60 patients found increased outliers with the use of PSI. Parratte *et al*^[27] suggested that more refinement needed to be done in PSI to have better control of

Table 2 Comparison of computerized tomography based and magnetic resonance imaging based patient specific blocks

	Computerized tomography based blocks	Magnetic resonance imaging based blocks
Time for study	Lesser (approximately 5 min)	Longer (approximately 45 min)
Cost	Economical	Costlier
Radiation exposure	Uses ionizing radiation. But focused hip-knee-ankle computerized tomography scanogram reduces exposure to 5 mSv (equal to yearly background exposure)	Does not use ionizing radiation
Availability	Easily available	Not available at all centers
Patient turn over	Useful for high patient turnover centers	Not suitable for high patient turnover center
Contraindication	Can be used in patient with any metal prosthesis <i>in situ</i>	Cannot be used in patient with metal prosthesis or cardiac pacemaker <i>in situ</i>
Based on	Bony landmarks	Cartilage
Accuracy	Comparable	Comparable
Initial infrastructure set up cost	Lower as compared to MRI	High, non affordable for low volume centres
Claustrophobia	No contraindication	Can not be performed in claustrophobic patients

MRI: Magnetic resonance imaging.

the tibial rotation. The inferior results in these studies could have been due to the evolving technology of PSI at the time of these studies, the associated learning curve and different designs of the cutting jig used in the studies^[16,25,26].

The other point of discussion in the use of PSI is the radiological method used for pre-operative planning. This technology utilizes advanced imaging techniques like magnetic resonance imaging (MRI) and CT scan to reproduce a 3D model of the patient's bone which is in turn used to create jigs which are used intra-operatively either to directly take bone cuts or to guide the insertion of pins. The debate regarding the best imaging modality is ongoing. In a systematic review of the use of CT vs MRI in PSI showed a decreased number of outliers in the CT group (12.5%) as compared to MRI (16.9%) group^[28]. There are various advantages of the CT-based PSI over MRI-based (Table 2). The CT scan is associated with decreased cost and imaging times^[28]. Moreover, it can be easily performed in patients with cardiac pacemakers and metallic implant *in situ*. The widespread availability of the CT scan in a developing country, also make it accessible to a larger profile of surgeons and patients. Even in high volume center, there is usually a single MRI machine which can further increase the waiting period of the patient. The accuracy of the CT-based PSI as compared to the MRI-based PSI have been found to be comparable^[29,30]. The only disadvantage of the CT scan based PSI is the possibility of increased radiation exposure as compared to MRI. This has further been circumvented by the use of focused scans of the hip, knee and ankle, which further decreases the dosage of radiation to 5MSv, which is comparable to the background radiation or approximately 70 chest X-rays^[31]. In the present study, CT-based PSI technique was used and found to provide a satisfactory outcome.

In the present study, we found more accurate alignment in TKA done by PSI compared to CI, with a statistically significant improvement in MFT angle in PSI group ($P = 0.001$). The number of outliers was also

decreased with the use of PSI. The mean MFT angle measured postoperatively in group 1 was 178.23° and in group 2 it was 175.73°. The preoperative planning done in PSI group was the main reason for achieving accurate MA postoperatively. The CT scanogram of lower limb done preoperatively gives thorough information of actual bony anatomy of knee and limb alignment. The patient specific blocks thus produced fit to patient's bony anatomy accurately and thus lead to proper pin positioning and accurate bone cuts intraoperatively. Proper pin positioning, and accurate bone cuts can be attributed as the reasons for the improvement in mechanical alignment in TKA with PSI.

PSI avoids manual error involved in pin position with conventional instruments. The accuracy of the valgus cut angle depends on an accurate entry point and the snug fit of the intra-medullary alignment rod in the femoral canal. These two factors are circumvented by the use of PSI and hence may be responsible for better achievement of the distal femoral valgus angle. Moreover, the positioning of the extra-medullary alignment rod for the tibia depends on the surgeon's perception of centralizing the rod at the center of the ankle. This is subject to error due to the surgeon (difference in perception of the alignment) and also due to patient factors like excessive fat and soft tissue around the ankle, *etc.* With the use of PSI, both these factors are decided pre-operatively during planning and hence the manual error is minimized.

There were certain shortcomings of the present study. The study was not a randomized controlled trial. Our sample size was also small, but it can be considered a representative study and further studies should be done to define the exact efficacy of PSI in improving the overall mechanical axis.

Considering the current trends of joint replacement and also due to a consistent increase in the life expectancy of the population, there is going to be an exponential growth in the number of total knee arthroplasty being done. The focus is shifting to increase the long-term survival of the artificial joints in a cost efficient manner, to decrease the financial and health burden of revision

surgery. PSI technology is a step in this direction as it helps in improving the postoperative mechanical axis and also improve the operating room efficiency. This study defines that the PSI technology helps in significantly improving the postoperative mechanical alignment as compared to conventional technology and has future potential to provide long-term benefits to patients.

COMMENTS

Background

The zeal to achieve improved patient outcomes and longer implant survival has opened new avenues in the field of total knee arthroplasty. Patient specific jigs hold promise in achieving both these.

Research frontiers

Patient specific blocks have recently caught the attention of researchers with multiple studies showing good results. These blocks can be manufactured on the basis of the patient's magnetic resonance imaging (MRI) and computer tomography (CT) scan. It is of interest to see whether CT based jigs can achieve good results in the post operative outcomes and alignment of patients undergoing total knee arthroplasty.

Innovations and breakthroughs

The authors confirm that CT based blocks can achieve accurate restoration of the post operative mechanical axis and good post operative pain relief and rehabilitation. The CT scan based blocks hold some inherent advantages over the MRI based jigs and these have also been discussed in the present study.

Applications

CT based patient specific blocks hold promise for the future in the quest to improve implant longevity in total knee arthroplasty.

Peer-review

This manuscript is well organized, and the results are acceptable.

REFERENCES

- 1 **Haritnian EG**, Pimpalnerkar AL. Computer Assisted Total Knee Arthroplasty: Does it Make a Difference? *Maedica* (Buchar) 2013; **8**: 176-181 [PMID: 24371482]
- 2 **Ritter MA**, Faris PM, Keating EM, Meding JB. Postoperative alignment of total knee replacement. Its effect on survival. *Clin Orthop Relat Res* 1994; **(299)**: 153-156 [PMID: 8119010]
- 3 **Sharkey PF**, Hozack WJ, Rothman RH, Shastri S, Jacoby SM. Insall Award paper. Why are total knee arthroplasties failing today? *Clin Orthop Relat Res* 2002; **(404)**: 7-13 [PMID: 12439231]
- 4 **Ng VY**, DeClaire JH, Berend KR, Gulick BC, Lombardi AV. Improved accuracy of alignment with patient-specific positioning guides compared with manual instrumentation in TKA. *Clin Orthop Relat Res* 2012; **470**: 99-107 [PMID: 21809150 DOI: 10.1007/s11999-011-1996-6]
- 5 **Whiteside LA**, Ohl MD. Tibial tubercle osteotomy for exposure of the difficult total knee arthroplasty. *Clin Orthop Relat Res* 1990; **(260)**: 6-9 [PMID: 2225644]
- 6 **Jerosch J**, Peuker E, Philipps B, Filler T. Interindividual reproducibility in perioperative rotational alignment of femoral components in knee prosthetic surgery using the transepicondylar axis. *Knee Surg Sports Traumatol Arthrosc* 2002; **10**: 194-197 [PMID: 12012038]
- 7 **Higuera CA**, Deirmengian C. The new technologies in knee arthroplasty. *J Clin Rheumatol* 2012; **18**: 345-348 [PMID: 23047534 DOI: 10.1097/RHU.0b013e3182724079]
- 8 **Tibesku CO**, Innocenti B, Wong P, Salehi A, Labey L. Can CT-based patient-matched instrumentation achieve consistent rotational alignment in knee arthroplasty? *Arch Orthop Trauma Surg* 2012; **132**: 171-177 [PMID: 22006572 DOI: 10.1007/s00402-011-1406-2]
- 9 **Bardakos N**, Cil A, Thompson B, Stocks G. Mechanical axis cannot be restored in total knee arthroplasty with a fixed valgus resection angle: a radiographic study. *J Arthroplasty* 2007; **22**: 85-89 [PMID: 17823023]
- 10 **Hinarejos P**, Corrales M, Matamalas A, Bisbe E, Cáceres E. Computer-assisted surgery can reduce blood loss after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 356-360 [PMID: 19083205 DOI: 10.1007/s00167-008-0683-y]
- 11 **Moon YW**, Han JH, Lee KH, Jang SW, Seo JG. Clinical Outcome of IM-Guided Total Knee Arthroplasty with Inappropriate Femoral Resection in Coronal Plane. *Knee Surg Relat Res* 2013; **25**: 19-24 [PMID: 23508201 DOI: 10.5792/ksr.2013.25.1.19]
- 12 **Schnurr C**, Csécssei G, Eysel P, König DP. The effect of computer navigation on blood loss and transfusion rate in TKA. *Orthopedics* 2010; **33**: 474 [PMID: 20608630 DOI: 10.3928/01477447-20100526-08]
- 13 **Bae DK**, Song SJ. Computer assisted navigation in knee arthroplasty. *Clin Orthop Surg* 2011; **3**: 259-267 [PMID: 22162787 DOI: 10.4055/cios.2011.3.4.259]
- 14 **Cheng T**, Pan XY, Mao X, Zhang GY, Zhang XL. Little clinical advantage of computer-assisted navigation over conventional instrumentation in primary total knee arthroplasty at early follow-up. *Knee* 2012; **19**: 237-245 [PMID: 22130355 DOI: 10.1016/j.knee.2011.10.001]
- 15 **Hamilton WG**, Parks NL, Saxena A. Patient-specific instrumentation does not shorten surgical time: a prospective, randomized trial. *J Arthroplasty* 2013; **28**: 96-100 [PMID: 23910821 DOI: 10.1016/j.arth.2013.04.049]
- 16 **Chen JY**, Yeo SJ, Yew AK, Tay DK, Chia SL, Lo NN, Chin PL. The radiological outcomes of patient-specific instrumentation versus conventional total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 630-635 [PMID: 23996069 DOI: 10.1007/s00167-013-2638-1]
- 17 **Barrack RL**, Ruh EL, Williams BM, Ford AD, Foreman K, Nunley RM. Patient specific cutting blocks are currently of no proven value. *J Bone Joint Surg Br* 2012; **94**: 95-99 [PMID: 23118393 DOI: 10.1302/0301-620X.94B11.30834]
- 18 **Stronach BM**, Pelt CE, Erickson J, Peters CL. Patient-specific total knee arthroplasty required frequent surgeon-directed changes. *Clin Orthop Relat Res* 2013; **471**: 169-174 [PMID: 22956239 DOI: 10.1007/s11999-012-2573-3]
- 19 **Scholes C**, Sahni V, Lustig S, Parker DA, Coolican MR. Patient-specific instrumentation for total knee arthroplasty does not match the pre-operative plan as assessed by intra-operative computer-assisted navigation. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 660-665 [PMID: 24042965 DOI: 10.1007/s00167-013-2670-1]
- 20 **Vaishya R**, Singh AP, Vaish A. Outcome of subvastus approach in elderly nonobese patients undergoing bilateral simultaneous total knee arthroplasty: A randomized controlled study. *Indian J Orthop* 2013; **47**: 430-431 [PMID: 23960295 DOI: 10.4103/0019-5413.114948]
- 21 **Lotke PA**, Ecker ML. Influence of positioning of prosthesis in total knee replacement. *J Bone Joint Surg Am* 1977; **59**: 77-79 [PMID: 833180]
- 22 **Hafez MA**, Chelule KL, Seedhom BB, Sherman KP. Computer-assisted total knee arthroplasty using patient-specific templating. *Clin Orthop Relat Res* 2006; **444**: 184-192 [PMID: 16446589]
- 23 **Heyse TJ**, Tibesku CO. Improved femoral component rotation in TKA using patient-specific instrumentation. *Knee* 2014; **21**: 268-271 [PMID: 23140905 DOI: 10.1016/j.knee.2012.10.009]
- 24 **Renson L**, Poilvache P, Van den Wyngaert H. Improved alignment and operating room efficiency with patient-specific instrumentation for TKA. *Knee* 2014; **21**: 1216-1220 [PMID: 25450010 DOI: 10.1016/j.knee.2014.09.008]
- 25 **Abane L**, Anract P, Boisgard S, Descamps S, Courpied JP, Hamadouche M. A comparison of patient-specific and conventional instrumentation for total knee arthroplasty: a multicentre randomised controlled trial. *Bone Joint J* 2015; **97-B**: 56-63 [PMID: 25568414 DOI: 10.1302/0301-620X.97B1.34440]
- 26 **Klatt BA**, Goyal N, Austin MS, Hozack WJ. Custom-fit total knee

- arthroplasty (OtisKnee) results in malalignment. *J Arthroplasty* 2008; **23**: 26-29 [PMID: 18165024 DOI: 10.1016/j.arth.2007.10.001]
- 27 **Parratte S**, Blanc G, Boussemart T, Ollivier M, Le Corroller T, Argenson JN. Rotation in total knee arthroplasty: no difference between patient-specific and conventional instrumentation. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2213-2219 [PMID: 23942938 DOI: 10.1007/s00167-013-2623-8]
- 28 **Stirling P**, Valsalan Mannambeth R, Soler A, Batta V, Malhotra RK, Kalairajah Y. Computerised tomography vs magnetic resonance imaging for modeling of patient-specific instrumentation in total knee arthroplasty. *World J Orthop* 2015; **6**: 290-297 [PMID: 25793170 DOI: 10.5312/wjo.v6.i2.290]
- 29 **Cenni F**, Timoncini A, Ensini A, Tamarri S, Belvedere C, D'Angeli V, Giannini S, Leardini A. Three-dimensional implant position and orientation after total knee replacement performed with patient-specific instrumentation systems. *J Orthop Res* 2014; **32**: 331-337 [PMID: 24174168 DOI: 10.1002/jor.22513]
- 30 **Ensini A**, Timoncini A, Cenni F, Belvedere C, Fusai F, Leardini A, Giannini S. Intra- and post-operative accuracy assessments of two different patient-specific instrumentation systems for total knee replacement. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 621-629 [PMID: 24061719 DOI: 10.1007/s00167-013-2667-9]
- 31 **Koch P**. MyKnee system: a new vision in total knee replacement. *Maitrise Orthopédique* 2011; **2**: 32-35. Available from: URL: <http://orthopaedie-unfallchirurgie.universimed.com/artikel/myknee-system-new-vision-total-knee-replacement>

P- Reviewer: Camera A, Fujimoto E **S- Editor:** Kong JX
L- Editor: A **E- Editor:** Wu HL



Retrospective Cohort Study

Constrained fixed-fulcrum reverse shoulder arthroplasty improves functional outcome in epileptic patients with recurrent shoulder instability

Tanujan Thangarajah, Deborah Higgs, J I L Bayley, Simon M Lambert

Tanujan Thangarajah, Deborah Higgs, J I L Bayley, Simon M Lambert, the Shoulder and Elbow Service, the Royal National Orthopaedic Hospital, Stanmore HA7 4LP, United Kingdom

Author contributions: Thangarajah T contributed to data collection, data analysis, and manuscript preparation; Higgs D, Bayley JIL and Lambert SM carried out surgeries and critical analysis of manuscript.

Institutional review board statement: This retrospective study was undertaken using data from medical records only and thus was conducted without IRB approval.

Informed consent statement: Our retrospective study contained data from medical records.

Conflict-of-interest statement: The authors declare that they have no conflict of interest. No benefits in any form have been received or will be received from any commercial party related directly or indirectly to the subject of this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Tanujan Thangarajah, Specialist Trainee Year 5, the Shoulder and Elbow Service, the Royal National Orthopaedic Hospital, Stanmore HA7 4LP, United Kingdom. tanujan1@hotmail.com
Telephone: +44-20-89542300

Received: January 12, 2016

Peer-review started: January 14, 2016

First decision: February 29, 2016

Revised: May 4, 2016

Accepted: May 7, 2016

Article in press: May 9, 2016

Published online: July 18, 2016

Abstract

AIM: To report the results of fixed-fulcrum fully constrained reverse shoulder arthroplasty for the treatment of recurrent shoulder instability in patients with epilepsy.

METHODS: A retrospective review was conducted at a single facility. Cases were identified using a computerized database and all clinic notes and operative reports were reviewed. All patients with epilepsy and recurrent shoulder instability were included for study. Between July 2003 and August 2011 five shoulders in five consecutive patients with epilepsy underwent fixed-fulcrum fully constrained reverse shoulder arthroplasty for recurrent anterior shoulder instability. The mean duration of epilepsy in the cohort was 21 years (range, 5-51) and all patients suffered from grand mal seizures.

RESULTS: Mean age at the time of surgery was 47 years (range, 32-64). The cohort consisted of four males and one female. Mean follow-up was 4.7 years (range, 4.3-5 years). There were no further episodes of instability, and no further stabilisation or revision procedures were performed. The mean Oxford shoulder instability score improved from 8 preoperatively (range, 5-15) to 30 postoperatively (range, 16-37) ($P = 0.015$) and the mean subjective shoulder value improved from 20 (range, 0-50) preoperatively to 60 (range, 50-70) postoperatively ($P = 0.016$). Mean active forward elevation improved from 71° preoperatively (range,

45°-130°) to 100° postoperatively (range, 80°-90°) and mean active external rotation improved from 15° preoperatively (range, 0°-30°) to 40° (20°-70°) postoperatively. No cases of scapular notching or loosening were noted.

CONCLUSION: Fixed-fulcrum fully constrained reverse shoulder arthroplasty should be considered for the treatment of recurrent shoulder instability in patients with epilepsy.

Key words: Arthroplasty; Dislocation; Epilepsy; Instability; Shoulder

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Epileptic patients with recurrent shoulder instability pose a significant challenge. We have reported the first series in the literature of patients with epilepsy-related recurrent shoulder instability to be treated with fixed-fulcrum constrained reverse anatomy arthroplasty. Our results suggest that it is successful in reducing pain and eliminating actual and perceived instability in this population. Contrary to previous reports there were no cases of glenoid loosening, implant failure or revision procedures. Postoperatively, there was a significant improvement in functional outcome, which was accompanied by a mean improvement of 25° in active external rotation and 29° in active forward flexion.

Thangarajah T, Higgs D, Bayley JIL, Lambert SM. Constrained fixed-fulcrum reverse shoulder arthroplasty improves functional outcome in epileptic patients with recurrent shoulder instability. *World J Orthop* 2016; 7(7): 434-441 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/434.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.434>

INTRODUCTION

Epileptic seizures can cause shoulder dislocation and instability^[1]. The incidence of dislocation during a seizure is approximately 0.6% but this is likely to be an underestimation since many may be undetected because medical management of the seizure often takes precedence^[2,3]. Recurrent instability is common and occurs soon after the first dislocation, with anterior and posterior instability occurring equally^[1]. Significant bone loss from the glenoid rim and fossa, and corresponding extensive humeral head fractures are held responsible for this and are recognized as being a hallmark of the condition^[1,4,5]. To address this, the majority of non-arthroplasty ("conservative") surgical strategies focus on restoration and/or augmentation of the bony glenohumeral joint while also addressing capsular insufficiency and arthritis^[6,7]. Despite technically satisfactory reconstruction ("preservative") procedures

some patients still experience persistent instability and increasing arthritis symptoms. Further conservative reconstruction becomes an unenviable prospect due to poor bone stock, large joint surface defects, and rotator cuff musculotendinous and capsular insufficiency. The patients are often young, in education or seeking work, and find the prospect of living with a painful unstable shoulder unbearable. In this context, arthrodesis has been reported to be a successful treatment strategy but the limitation in range of movement that inevitably results means that it is not suitable for all patients^[8]. Constrained arthroplasty may therefore represent an alternative treatment option.

The Bayley-Walker shoulder (Stanmore Implants Worldwide Ltd, United Kingdom) was specifically conceived for the treatment of patients with difficult shoulder reconstruction problems such as advanced rotator cuff arthropathy and tumours^[9,10]. The device is a constrained fixed-fulcrum reverse anatomy prosthesis comprising a large-pitched, hydroxy-apatite-coated titanium glenoid screw with a 22 mm CoCrMo alloy head that forms a constrained "snap-fit" articulation (to increase stability) with an UHMWPE liner encased in a tapered titanium alloy humeral component giving 60° of intrinsic motion in any direction^[10]. The center of rotation is placed medially and distally to the axis of the normal shoulder, which increases the lever arm of the deltoid, but to a lesser degree than most existing non-linked reverse anatomy prostheses^[9]. These features make the Bayley-Walker prosthesis a potential treatment option for recurrent shoulder instability in patients with epilepsy who have sufficient glenoid bone stock for secure primary fixation of the glenoid component. There are no reports of this management strategy in the current published literature.

The aim of this retrospective study was to report the results of fixed-fulcrum fully constrained reverse shoulder arthroplasty (FF-RSA) for the treatment of recurrent shoulder instability in patients with epilepsy.

MATERIALS AND METHODS

Between July 2003 and August 2011 five shoulders in five consecutive patients with epilepsy underwent FF-RSA for recurrent instability. Cases were identified using a computerized database and all clinic notes and operative reports were reviewed. The mean duration of epilepsy in the cohort was 21 years (range, 5-51) and all patients suffered from grand mal seizures. The index dislocation occurred a mean of 15 years (range, 2-38) before FF-RSA surgery. All cases were performed by the senior authors (J I L Bayley, Deborah Higgs, and Simon M Lambert). Mean age at the time of surgery was 47 years (range, 32-64) and the cohort consisted of four males and one female. All patients had anterior instability. Three patients had bilateral symptoms. The dominant shoulder was affected in three cases. FF-RSA was performed after an average of two previous

Table 1 Patient details

Case	Gender	Age	Previous stabilisation procedures	Duration of follow-up (yr)	Additional procedures
1	Male	41	Putti-Platt procedure; Allograft humeral head reconstruction; Coracoid transfer; Revision allograft humeral head reconstruction	4.3	-
2	Female	64	Coracoid transfer	4.6	-
3	Male	48	No previous stabilisation procedures	4.8	-
4	Male	32	Putti-Platt procedure; Bankart repair; Revision Bankart repair; Allograft humeral head reconstruction; Humeral head resurfacing	5.0	Examination under anaesthesia and arthrocentesis due to persistent pain
5	Male	51	No previous stabilisation procedures	-	-

stabilisation procedures (range, 0-5) in all but two patients in whom the procedure was used as primary treatment (Cases 3 and 5). All patients had had an onset of instability that coincided with a seizure. In all cases subsequent dislocations occurred during normal activities or further seizures.

The indication for surgery was severe pain and recurrent or persistent (*i.e.*, the shoulder was never able to be actively centralised) instability with a non-functioning rotator cuff. The glenoid bone stock was judged on computer tomography (CT) to be sufficient for primary implantation of the glenoid screw component. Neurological advice was sought preoperatively in all cases to optimise the treatment of the epilepsy. Detailed patient data are presented in Table 1.

Surgical technique

The deltopectoral approach was used in all patients. The glenoid was exposed and a Bayley-Walker uncemented glenoid screw was inserted using standard instrumentation. The humeral canal was prepared, and a Bayley-Walker humeral stem was inserted. A simple sling was used for 6 wk postoperatively during which period passive rotation at waist level was permitted; active scapular postural and motion exercises were encouraged. An active anterior deltoid activation programme was initiated after the first phase when osseo-integration of the glenoid screw was considered likely to have been achieved.

Assessment of radiological and functional outcome

Preoperative and postoperative radiographic imaging was performed in all cases and included anteroposterior and axillary views. Scapular notching was classified by the size of the defect on the anteroposterior radiograph using the four-part grading system devised by Sirveaux *et al.*^[11]. Humeral loosening was assessed from anteroposterior radiographs as described by Boileau *et al.*^[12].

Preoperative and postoperative clinical outcome measures included active forward elevation, active external rotation, and the Oxford Shoulder Instability score (OSIS)^[13]. Range of movement was assessed by

the operating surgeon and/or an orthopaedic resident. The OSIS is a 12-item questionnaire that places a significant emphasis on the impact the patient's shoulder instability has on their lives, making it a highly discriminant tool to assess the efficacy of interventions used to treat it. In addition, all patients were assessed using the subjective shoulder value (SSV). The SSV can be used as a supplementary tool to traditional, more complex outcome measures and may be used in conjunction with other scores to assess the patients' outcome. It has also been suggested to be a more sensitive measure of shoulder function in patients with instability^[14].

Statistical analysis

The paired *t* test was used to compare OSIS and SSV before and after surgery. A *P* value of < 0.05 was considered significant. The SPSS software package, version 22 (SPSS Inc, an IBM Company, Chicago, Illinois) was used to analyse data.

RESULTS

Mean follow-up was 4.7 years (range, 4.3-5 years). One patient was deceased (Case 5) and was therefore exempt from functional outcome analysis. There were no further episodes of instability or persistence of apprehension, and no further stabilisation procedures and no revision procedures were performed. All patients were on medical treatment for their epilepsy and had been reviewed by a neurologist preoperatively. No cases of scapular notching or loosening of either the humeral or glenoid component were noted.

Mean active forward elevation improved from 71° preoperatively (range, 45°-130°) to 100° postoperatively (range, 80°-90°) (*P* = 0.418). Mean active external rotation improved from 15° preoperatively (range, 0°-30°) to 40° (20°-70°) postoperatively (*P* = 0.221). Clinical outcome following constrained fixed-fulcrum reverse shoulder arthroplasty can be found in Table 2.

The mean OSIS improved from 8 preoperatively (range, 5-15) to 30 postoperatively (range, 16-37) (*P* = 0.015). The mean SSV improved from 20 (range, 0-50)

Table 2 Clinical outcome following constrained fixed-fulcrum reverse shoulder arthroplasty

Case	Active forward elevation in degrees (preop/postop)	Active external rotation in degrees (preop/postop)	Oxford shoulder instability score (preop/postop)	Subjective shoulder value (preop/postop)
1	130/80	30/25	5/32	0/60
2	45/80	20/20	15/37	50/70
3	60/90	10/70	6/33	20/60
4	50/150	0/45	7/16	10/50

Preop: Pre operation; Postop: Post operation.

preoperatively to 60 (range, 50-70) postoperatively ($P = 0.016$). Following surgery all patients reported less pain and avoided fewer activities due to the fear of a further dislocation. An improvement in dressing and washing was also noted in all cases. The results from the OSIS are summarized in Table 3.

One patient (Case 4) complained of persistent pain and underwent arthrocentesis to exclude an infective cause. No organisms were isolated and the patient reported an excellent outcome at the latest follow-up characterized by an improvement in functional outcome.

Case presentations

Case 1: A 41-year-old male with epilepsy was evaluated for a painful and unstable glenohumeral joint eight years after the index dislocation. Four previous stabilisation procedures had been performed, but due to persistent symptoms FF-RSA was undertaken. Following surgery, there was a reduction in pain and an improvement in range of movement due to a stable glenohumeral joint. No prosthetic complications were noted at the latest follow-up (Figure 1).

Case 2: A 64-year-old female epileptic with a 38-year history of glenohumeral instability was reviewed for an unstable shoulder and severe pain. Preoperative CT demonstrated advanced osteoarthritis with subchondral cysts, subchondral sclerosis, and narrowed joint space. FF-RSA was carried out successfully with no implant-related complications. At the latest follow-up, instability had been eliminated and there was a concomitant reduction in pain, and an improvement in function.

Case 3: A 48-year-old male with epilepsy was assessed for a painfully unstable glenohumeral joint two years after the first dislocation. No previous stabilisation procedures had been performed. FF-RSA was undertaken in the setting of an inactive rotator cuff and functioning deltoid. Postoperatively, there were no episodes of instability and the patient was satisfied with the outcome (Figure 2).

Case 4: A 32-year-old epileptic male was reviewed following an 11-year history of glenohumeral instability. Five previous surgeries had been undertaken, including



Figure 1 Anteroposterior radiograph of a 41-year-old right hand-dominant male with 4 previous stabilizations, 4 years after a right Bayley-Walker fixed-fulcrum constrained reverse shoulder arthroplasty.

a humeral head resurfacing arthroplasty for dislocation arthropathy. FF-RSA was considered due to ongoing symptoms. At the time of surgery, the humeral head resurfacing implant was loose and there were arthritic changes on the glenoid. One year following surgery the patient complained of persistent pain and so arthrocentesis was undertaken. This did not demonstrate any infective cause and the pain eventually settled (Figure 3).

Case 5: A 51-year-old epileptic male was evaluated following a 16-year history of recurrent glenohumeral instability. No previous stabilisation procedures had been undertaken. At the time of surgery, a full-thickness rotator cuff tear was noted. No implant-related complications were detected following surgery. However, the patient later died of an unrelated medical condition.

DISCUSSION

Shoulder instability can be a significant problem in patients with epilepsy. Management is challenging as seizures exert considerable forces on surgical repairs. It is therefore imperative that a neurologist is involved preoperatively so that medical treatment can be optimized. Patients with epilepsy are prone to recurrence and often undergo multiple operations to achieve a stable shoulder joint^[1]. With each successive procedure the risk of complications increases and the chance of a successful outcome is reduced. Only a small proportion of cases remain refractory to conventional surgery but these patients often have distorted anatomy and multiple soft tissue defects that make further reconstruction challenging and fraught with complications. To address this, Thangarajah *et al*^[8] reported the outcome of six epileptic patients with recurrent instability followed-up for a mean of 39 mo who were treated with glenohumeral arthrodesis. Mean age of the cohort was 31 years. An overall improvement

Table 3 Change in the Oxford Shoulder Instability score following constrained fixed-fulcrum reverse shoulder arthroplasty

Item	No. of patients reporting an improvement	No. of patients reporting worsening	No. of patients reporting no change
No. of dislocations	4	0	0
Dressing oneself	4	0	0
Worst pain	4	0	0
Interference with work	4	0	0
Avoidance of activities due to fear of dislocation	4	0	0
Prevented activities of importance	4	0	0
Interference with social life	3	0	1
Interference with sport/hobbies	1	0	3
Frequency with which patient thinks about their shoulder	3	0	1
Willingness to lift heavy objects	1	0	3
Base-line level of pain in shoulder	4	0	0
Avoidance of certain positions when sleeping	2	0	2

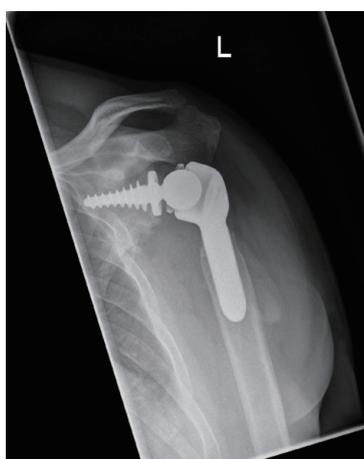


Figure 2 Anteroposterior radiograph of a 48-year-old left hand-dominant male, one year after a left Bayley-Walker fixed-fulcrum constrained reverse shoulder arthroplasty.



Figure 3 Anteroposterior radiograph of a 32-year-old right hand-dominant male with 5 previous stabilizations, 3 years after a left Bayley-Walker fixed-fulcrum constrained reverse shoulder arthroplasty.

in functional outcome was noted, predominantly due to the reduction in pain and elimination of instability, but due to the restriction in range of movement and limitation in function it could not be recommended ubiquitously. In this context, constrained shoulder arthroplasty could be a potential alternative but there are no studies examining this strategy in an epileptic population.

Constrained shoulder arthroplasty is characterised by mechanical coupling of the humeral and glenoid components around a fixed center of rotation (hence the terminology “fixed-fulcrum” total shoulder arthroplasty). FF-RSA was initially considered as a potential solution for rotator cuff arthropathy but early designs were associated with loosening and implant failure, with relatively poor ranges of motion compared with the emerging anatomical designs^[15,16].

The Bayley-Walker shoulder replacement is a constrained FF-RSA device that has been used for complex reconstruction problems in which the rotator cuff is absent (proximal humeral tumour excision), severely deficient (rotator cuff arthropathy), or likely to be compromised with the passage of time (post-traumatic

arthropathy, particularly when associated with disruption of the coraco-acromial arch)^[9,10]. Its design includes a conical shaped glenoid screw that reduces the strain placed on the implant, and “snap-fit” components that enhance stability and place the center of rotation medially and distally to the axis of the normal shoulder in order to increase the lever arm of the abductors^[9,17].

Post *et al*^[18] reported the results of 43 constrained total shoulder replacements performed in 42 patients. Follow-up was for a minimum of 27 mo. Indications for surgery included osteonecrosis, complex fractures, juvenile rheumatoid arthritis, and failed arthroplasty. Twelve material failures were noted in 22 stainless steel implants but only two were found in 21 cobalt-chromium prostheses. Glenoid loosening was not encountered. Traumatic dislocation occurred in four cases. Revision surgery was undertaken in 13 patients and was due to further traumatic episodes causing dislocation and material failure. Maintenance of the glenoid vault was found to be essential for secure fixation of the glenoid component and so the authors discouraged the use of constrained arthroplasty in conditions that caused excessive bone loss such as

tumours and severe osteoporosis. Coughlin *et al.*^[19] evaluated the results of 16 semi-constrained total shoulder arthroplasties performed for intractable pain and severe degenerative disease. Follow-up was for a mean of 31 mo, with one failure due to mechanical loosening. An improvement was noted in total range of motion. Griffiths *et al.*^[10] reviewed a series of 68 consecutive patients who underwent replacement of the proximal humerus for tumour using a massive endoprosthesis. The mean age of the group was 46 years and follow-up was for a mean of 5 years 11 mo. An unconstrained endoprosthesis was implanted into the first 64 patients and a custom-made constrained (Bayley-Walker) reverse polarity fixed-fulcrum implant linked to a massive proximal humeral endoprosthesis was used in the remaining four. No dislocations were noted in the group with a constrained implant at a mean of 14.5 mo following surgery. This was in contrast to the unconstrained group who had a dislocation rate of 25.9%. No cases of glenoid loosening were identified in the cohort.

Reverse total shoulder arthroplasty (RTSA) has been established as an effective treatment for rotator cuff arthropathy in an older patient population with low functional demands^[20]. Few studies have examined its use in patients under the age of 60 years with those that do reporting serious complications in the short-term such as the need for revision and dislocation^[21,22]. Muh *et al.*^[21] retrospectively reviewed 66 patients with a mean age of 52 years who underwent RTSA. Prior surgical procedures were common with 67% of the cohort having at least one prior intervention. At a mean follow-up of 36.5 mo there was an improvement in range of movement and functional outcome. Ten complications were identified including five dislocations that required revision in three cases and three infections that required further surgery. Scapular notching was found in 43% of patients. Sershon *et al.*^[22] evaluated 35 patients with a mean age of 54 years that underwent RTSA for a range of indications such as rheumatoid arthritis, failed rotator cuff repair, instability sequelae and cuff tear arthropathy. Of these, 83% had previous surgery averaging 2.5 procedures per patient. At a mean follow-up of 2.8 years there was an improvement in range of movement and functional outcome. Six patients had major complications including three dislocations, one subluxation and two fractures. Furthermore, three patients had revision surgery at 2 mo, 6 mo and 2.8 years.

Younger patients requiring shoulder arthroplasty present several challenges as they have higher functional demands and require longer implant survival when compared to elderly patients. In our series, FF-RSA was used in patients with a mean age of 47 years. At short-term follow up there was an improvement in functional outcome with no dislocations or revisions. This suggests that FF-RSA may be able to overcome some of the problems associated with more traditional

reverse anatomy designs and provide a suitable alternative to invasive fusion surgery in a younger population. However, further long-term studies are required because clinical outcomes have been noted to deteriorate with time following RTSA^[23].

We have reported the first series in the literature of patients with epilepsy-related recurrent shoulder instability to be treated with fixed-fulcrum constrained reverse anatomy arthroplasty. Our results suggest that it is successful in reducing pain and eliminating actual and perceived instability in this population. Contrary to previous reports there were no cases of glenoid loosening, implant failure or revision procedures. Post-operatively, there was a significant improvement in functional outcome as illustrated by an increase in the OSIS and SSV. This was accompanied by a mean improvement of 25° in active external rotation and 29° in active forward flexion. This is in contrast to other studies in which limitation of active external rotation characterises reversed-polarity semi-constrained prostheses^[24-26]. We attribute our findings to the maintenance of teres minor and recruitment of the posterior deltoid, which can work more effectively against a fixed fulcrum with its less-medialised center of rotation^[27].

Limitations of this small cohort study include those associated with its retrospective design and the mean follow-up of 4.7 years, which is relatively short in terms of prosthesis survivorship. However, Uri *et al.*^[27] have shown that if a FF-RSA is becoming loose, it is usually apparent within this time frame. We believe that these prostheses can obtain durable fixation through secondary osseointegration even in the challenging environment of a patient in whom epilepsy is a concomitant problem. This study of a unique group of patients previously considered poor candidates for shoulder arthroplasty provides some evidence of the value of FF-RSA in the treatment of a difficult and relatively uncommon problem. Further prospective studies examining the performance of this implant in this and similarly challenging patient populations in which the stability of conventional reverse-polarity arthroplasty remains uncertain are warranted.

In conclusion, epileptic patients with recurrent shoulder instability pose a significant challenge. Traditional operative measures may be unsuccessful and multiple revisions are common. In our series, FF-RSA eliminated recurrent instability and significantly improved functional outcome. This was accompanied by an improvement in pain and range of movement (external rotation and forward flexion). When managing this complex patient group, medical optimisation is essential and we therefore recommend that a neurologist be involved at the earliest possible juncture.

COMMENTS

Background

Epileptic patients with recurrent shoulder instability pose a significant challenge. Significant bone loss from the glenoid and humeral head is a common finding.

Patients are often young, in education or seeking work, and find the prospect of living with a painful unstable shoulder unbearable. In this context, arthrodesis has been reported to be a successful treatment strategy but the limitation in range of movement that inevitably results means that it is not suitable for all patients. The purpose of this study was to report the results of fixed-fulcrum fully constrained reverse shoulder arthroplasty for the treatment of recurrent shoulder instability in patients with epilepsy.

Research frontiers

The authors have reported the first series in the literature of patients with epilepsy-related recurrent shoulder instability to be treated with fixed-fulcrum constrained reverse anatomy arthroplasty. This study of a unique group of patients previously considered poor candidates for shoulder arthroplasty provides some evidence of the value of fixed-fulcrum constrained reverse anatomy arthroplasty in the treatment of a difficult and relatively uncommon problem.

Innovations and breakthroughs

At a mean of 4.7 years follow-up, there were no further episodes of instability, and no further stabilisation or revision procedures were performed in the cohort. A significant improvement was noted in functional outcome, as assessed by the Oxford Shoulder Instability Score ($P = 0.015$) and Subjective Shoulder Value ($P = 0.016$). This was accompanied by a mean improvement of 25° in active external rotation and 29° in active forward flexion. No cases of scapular notching or loosening were noted.

Applications

Fixed-fulcrum fully constrained reverse shoulder arthroplasty should be considered for the treatment of recurrent shoulder instability in patients with epilepsy.

Peer-review

This is a well written paper regarding a very difficult clinical problem to manage.

REFERENCES

- Bühler M, Gerber C. Shoulder instability related to epileptic seizures. *J Shoulder Elbow Surg* 2002; **11**: 339-344 [PMID: 12195251 DOI: 10.1067/mse.2002.124524]
- DeToledo JC, Lowe MR. Seizures, lateral decubitus, aspiration, and shoulder dislocation: Time to change the guidelines? *Neurology* 2001; **56**: 290-291 [PMID: 11235662]
- Schulz TJ, Jacobs B, Patterson RL. Unrecognized dislocations of the shoulder. *J Trauma* 1969; **9**: 1009-1023 [PMID: 5358646]
- Provencher MT, Bhatia S, Ghodadra NS, Grumet RC, Bach BR, Dewing CB, LeClere L, Romeo AA. Recurrent shoulder instability: current concepts for evaluation and management of glenoid bone loss. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 133-151 [PMID: 21123597 DOI: 10.2106/jbjs.j.00906]
- Thangarajah T, Lambert S. The management of recurrent shoulder instability in patients with epilepsy: a 15-year experience. *J Shoulder Elbow Surg* 2015; **24**: 1723-1727 [PMID: 26119633 DOI: 10.1016/j.jse.2015.04.008]
- Hutchinson JW, Neumann L, Wallace WA. Bone buttress operation for recurrent anterior shoulder dislocation in epilepsy. *J Bone Joint Surg Br* 1995; **77**: 928-932 [PMID: 7593109]
- Raiss P, Lin A, Mizuno N, Melis B, Walch G. Results of the Latarjet procedure for recurrent anterior dislocation of the shoulder in patients with epilepsy. *J Bone Joint Surg Br* 2012; **94**: 1260-1264 [PMID: 22933500 DOI: 10.1302/0301-620x.94b9.29401]
- Thangarajah T, Alexander S, Bayley I, Lambert SM. Glenohumeral arthrodesis for the treatment of recurrent shoulder instability in epileptic patients. *Bone Joint J* 2014; **96-B**: 1525-1529 [PMID: 25371468 DOI: 10.1302/0301-620x.96b11.33754]
- Ahir SP, Walker PS, Squire-Taylor CJ, Blunn GW, Bayley JI. Analysis of glenoid fixation for a reversed anatomy fixed-fulcrum shoulder replacement. *J Biomech* 2004; **37**: 1699-1708 [PMID: 15388312 DOI: 10.1016/j.jbiomech.2004.01.031]
- Griffiths D, Gikas PD, Jowett C, Bayliss L, Aston W, Skinner J, Cannon S, Blunn G, Briggs TW, Pollock R. Proximal humeral replacement using a fixed-fulcrum endoprosthesis. *J Bone Joint Surg Br* 2011; **93**: 399-403 [PMID: 21357964 DOI: 10.1302/0301-620x.93b3.24421]
- Sirveaux F, Favard L, Oudet D, Huquet D, Walch G, Molé D. Grammont inverted total shoulder arthroplasty in the treatment of glenohumeral osteoarthritis with massive rupture of the cuff. Results of a multicentre study of 80 shoulders. *J Bone Joint Surg Br* 2004; **86**: 388-395 [PMID: 15125127]
- Boileau P, Gonzalez JF, Chuinard C, Bicknell R, Walch G. Reverse total shoulder arthroplasty after failed rotator cuff surgery. *J Shoulder Elbow Surg* 2009; **18**: 600-606 [PMID: 19481959 DOI: 10.1016/j.jse.2009.03.011]
- Dawson J, Fitzpatrick R, Carr A. The assessment of shoulder instability. The development and validation of a questionnaire. *J Bone Joint Surg Br* 1999; **81**: 420-426 [PMID: 10872358]
- Gilbart MK, Gerber C. Comparison of the subjective shoulder value and the Constant score. *J Shoulder Elbow Surg* 2007; **16**: 717-721 [PMID: 18061114 DOI: 10.1016/j.jse.2007.02.123]
- Nam D, Kepler CK, Neviasser AS, Jones KJ, Wright TM, Craig EV, Warren RF. Reverse total shoulder arthroplasty: current concepts, results, and component wear analysis. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 23-35 [PMID: 21189245 DOI: 10.2106/JBJS.J.00769]
- Post M, Jablon M. Constrained total shoulder arthroplasty. Long-term follow-up observations. *Clin Orthop Relat Res* 1983; **(173)**: 109-116 [PMID: 6825321]
- Mordecai SC, Lambert SM, Meswania JM, Blunn GW, Bayley IL, Taylor SJ. An experimental glenoid rim strain analysis for an improved reverse anatomy shoulder implant fixation. *J Orthop Res* 2012; **30**: 998-1003 [PMID: 22095751 DOI: 10.1002/jor.22015]
- Post M, Haskell SS, Jablon M. Total shoulder replacement with a constrained prosthesis. *J Bone Joint Surg Am* 1980; **62**: 327-335 [PMID: 7364806]
- Coughlin MJ, Morris JM, West WF. The semiconstrained total shoulder arthroplasty. *J Bone Joint Surg Am* 1979; **61**: 574-581 [PMID: 438245]
- Guery J, Favard L, Sirveaux F, Oudet D, Mole D, Walch G. Reverse total shoulder arthroplasty. Survivorship analysis of eighty replacements followed for five to ten years. *J Bone Joint Surg Am* 2006; **88**: 1742-1747 [PMID: 16882896 DOI: 10.2106/jbjs.e.00851]
- Muh SJ, Streit JJ, Wanner JP, Lenarz CJ, Shishani Y, Rowland DY, Riley C, Nowinski RJ, Edwards TB, Gobezie R. Early follow-up of reverse total shoulder arthroplasty in patients sixty years of age or younger. *J Bone Joint Surg Am* 2013; **95**: 1877-1883 [PMID: 24132362 DOI: 10.2106/jbjs.l.10005]
- Sershon RA, Van Thiel GS, Lin EC, McGill KC, Cole BJ, Verma NN, Romeo AA, Nicholson GP. Clinical outcomes of reverse total shoulder arthroplasty in patients aged younger than 60 years. *J Shoulder Elbow Surg* 2014; **23**: 395-400 [PMID: 24129052 DOI: 10.1016/j.jse.2013.07.047]
- Favard L, Levigne C, Nerot C, Gerber C, De Wilde L, Mole D. Reverse prostheses in arthropathies with cuff tear: are survivorship and function maintained over time? *Clin Orthop Relat Res* 2011; **469**: 2469-2475 [PMID: 21384212 DOI: 10.1007/s11999-011-1833-y]
- Werner CM, Steinmann PA, Gilbart M, Gerber C. Treatment of painful pseudoparesis due to irreparable rotator cuff dysfunction with the Delta III reverse-ball-and-socket total shoulder prosthesis. *J Bone Joint Surg Am* 2005; **87**: 1476-1486 [PMID: 15995114 DOI: 10.2106/jbjs.d.02342]
- Wall B, Nové-Josserand L, O'Connor DP, Edwards TB, Walch G. Reverse total shoulder arthroplasty: a review of results according to etiology. *J Bone Joint Surg Am* 2007; **89**: 1476-1485 [PMID: 17606786 DOI: 10.2106/jbjs.f.00666]
- Boulahia A, Edwards TB, Walch G, Baratta RV. Early results of a reverse design prosthesis in the treatment of arthritis of the shoulder in elderly patients with a large rotator cuff tear. *Orthopedics* 2002; **25**: 129-133 [PMID: 11866145]
- Uri O, Beckles V, Higgs D, Falworth M, Middleton C, Lambert

S. Increased-offset reverse shoulder arthroplasty for the treatment of failed post-traumatic humeral head replacement. *J Shoulder*

Elbow Surg 2014; **23**: 401-408 [PMID: 24090978 DOI: 10.1016/j.jse.2013.07.041]

P- Reviewer: Anand A, Fanter N, Garg B, Yamakado K
S- Editor: Kong JX **L- Editor:** A **E- Editor:** Wu HL



Retrospective Study

Trochanter/calcar preserving reconstruction in tumors involving the femoral head and neck

Hwan Seong Cho, Young-Kyun Lee, Yong-Chan Ha, Kyung-Hoi Koo

Hwan Seong Cho, Young-Kyun Lee, Kyung-Hoi Koo, Department of Orthopaedic Surgery, Seoul National University Bundang Hospital, Seongnam 463-707, South Korea

Yong-Chan Ha, Department of Orthopaedic Surgery, Chung-Ang University College of Medicine, Seoul 156-755, South Korea

Author contributions: Lee YK designed and performed the research and wrote the paper; Koo KH designed the research and supervised the report; Cho HS designed the research and contributed to the analysis; Cho HS, Lee YK, Ha YC and Koo KH provided clinical advice.

Institutional review board statement: The design and protocol of this retrospective study were approved by the institutional review board in Seoul National University Bundang Hospital.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: We have no financial relationships to disclose.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Young-Kyun Lee, MD, Department of Orthopaedic Surgery, Seoul National University Bundang Hospital, 82 Gumi-ro, 173 beon-gil, Bundang-gu, Seongnam 463-707, South Korea. ykleemd@gmail.com

Telephone: +82-31-7877204
Fax: +82-31-7874056

Received: March 3, 2016
Peer-review started: March 4, 2016
First decision: April 15, 2016
Revised: April 22, 2016
Accepted: May 10, 2016
Article in press: May 11, 2016
Published online: July 18, 2016

Abstract

AIM: To evaluate the results of hip reconstruction with extensive excision for tumor confined to the femoral head and neck.

METHODS: We designed a resection preserving the greater trochanter and lower portion of calcar femorale, and utilized conventional total hip prosthesis. We retrospectively reviewed 7 patients, who underwent a wide resection and reconstruction using conventional hip prosthesis. There were 3 men and 4 women and their mean age was 42.5 years (22 to 65 years). The histologic diagnosis of each patient was low-grade osteosarcoma, diffuse large B-cell lymphoma, liposclerosing myxofibroma, intraosseous lipoma, chondroblastoma, giant cell tumor and focal intramedullary fibrosis.

RESULTS: One patient with lymphoma died due to disease dissemination at 10 mo postoperatively and the remaining 6 patients were followed for a mean of 4.7 years (3 to 6 years). All patients were able to return to their daily activities and no patient had local recurrence. No radiographic signs of loosening, wear, and osteolysis were found at the last follow-up.

CONCLUSION: Trochanter/calcar-preserving resection

of the proximal femur and reconstruction using conventional total hip prosthesis, is a satisfactory treatment for tumors confined to the femoral head and neck.

Key words: Total hip arthroplasty; Reconstruction; Tumor; Femoral head

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This is a retrospective study to evaluate the results of trochanter and calcar preserving reconstruction in tumors involving the femoral head and neck. While usual osteotomy for primary total hip arthroplasty is made straightly at 0.5 inch above the lesser trochanter, we made a curved osteotomy in coronal plane from the tip of greater trochanter to lower level or below the lesser trochanter to remove the tumor lesion confined to femoral head and neck. This technique can preserve the greater trochanter and lower portion of the calcar femorale. This surgical technique is a satisfactory treatment for tumors confined to the femoral head and neck.

Cho HS, Lee YK, Ha YC, Koo KH. Trochanter/calcar preserving reconstruction in tumors involving the femoral head and neck. *World J Orthop* 2016; 7(7): 442-447 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/442.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.442>

INTRODUCTION

The proximal femur is a common site of primary malignant bone tumors, including chondrosarcoma, Ewing's sarcoma and osteosarcoma^[1]. An array of benign bone tumors; giant cell tumor, chondroblastoma, and clear cell chondrosarcoma may develop at the proximal femoral epiphysis and extend to the metaphysis^[2-4]. Intra-articular involvement is rare in these tumors, although they might occur following a pathologic fracture.

Patients with tumors confined to the femoral head have been candidates for curettage-bone graft^[5] or an extensive resection of the proximal femur and reconstruction, usually hemiarthroplasty, using tumor prosthesis depending on the biologic aggressiveness of the tumor^[6-8].

In the process of resection and reconstruction, the greater trochanter is osteomized or excised and after then, the greater trochanter or the insertion of the abductor muscle is attached to the tumor prosthesis with wires or cable grip, which can induce complications including wire or cable breakage, trochanteric fragment migration, nonunion, bursitis, and metallosis^[9-12].

Tumor prosthesis is highly costive. One more drawback of the tumor prosthesis is the difficulty on determining the actual length and width of the resected bone even with a use of modular endoprosthesis^[13].

Intermediate to long term survivorship of bipolar tumor prosthesis is not satisfactory compared to conventional total hip arthroplasty^[7,8,14].

Since 2007, we have treated tumors involving femoral head and neck using a trochanter/calcar-preserving resection and conventional total hip prosthesis. In this study, we present the operative technique and evaluate the results after trochanter-preserving resection with use of conventional prosthesis.

MATERIALS AND METHODS

The surgical treatment algorithm of tumors of the femoral head and neck at our department is as follows. The primary treatment for histologically-proven benign bone tumors confined to the femoral head and neck is curettage and bone graft^[5]. However: (1) when there is a suspicion of malignancy or solitary bone metastasis; (2) when there is a risk of superior retinacular or lateral epiphyseal arterial damage during the curettage and consequent develop of osteonecrosis; (3) when the lesion is large and located at the subchondral portion of the femoral head apex and consequent collapse is expected after the curettage; and (4) when there is a local recurrence after the curettage, we perform a trochanter/calcar-preserving resection of the proximal femur and reconstruction using conventional hip prostheses.

Tumors with a pathologic fracture, an involvement of the greater trochanter, involvement of the lesser trochanter, cortical penetration, or intra-articular involvement are treated with more extensive resection and reconstruction using revision prosthesis or tumor-prosthesis.

Between June 2007 and December 2011, 20 patients were operated due to tumors of the femoral head and neck at the authors' hospital. Among them, 13 patients were treated with curettage with bone graft (11 patients) or cement filling (2 patients). The remaining seven patients, who were operated with a trochanter-preserving resection of the proximal femur and total hip arthroplasty using conventional prosthesis, were subjects of this study.

There were 3 men (3 hips) and 4 women (4 hips), and the mean age at the time of operation was 42.5 years (range, 22 to 65 years). All patients presented with a pain of affected hip. The mean time interval between the onset of hip pain and the index operation was 13.6 mo (range, 1.3 to 48.1 mo).

We made preoperative diagnoses and evaluated the tumor extent on plain radiographs, computed tomography and/or magnetic resonance image. We planned a wide resection (≥ 1 cm from the tumor margin) bearing in mind the possibility of the malignant tumor (Figure 1).

All THAs were carried out by one surgeon. The patient was placed in a lateral position on the operating room table. A longitudinal posterolateral incision was made. Trochanteric bursa and underlying fat tissues

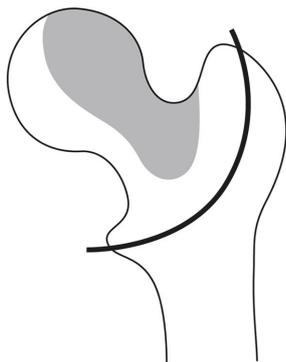


Figure 1 Preoperatively a wide resection margin was planned ≥ 1 cm from the tumor margin.

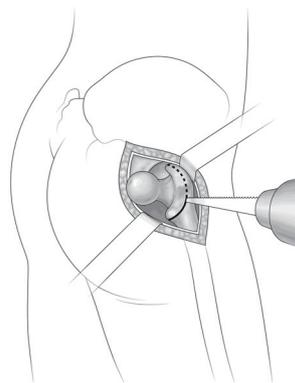


Figure 2 To obtain adequate resection margin from tumor, the curved osteotomy is performed from middle to lower portion of the lesser trochanter to the tip of greater trochanter.

were removed to expose short external rotators and sciatic nerve. External rotators were cut at their tendinous attachments to the trochanteric crest and the posterior capsule of the hip joint was incised. The femoral head was dislocated posteriorly.

To remove the diseased femoral head and neck, preserving the greater trochanter and lower portion of the calcar femorale, we made a curved osteotomy in coronal plane from the tip of greater trochanter to lower level or below the lesser trochanter according to the tumor margin while usual osteotomy for primary total hip arthroplasty is made straightly at 0.5 inch above lesser trochanter. The posterior cortex and endosteal cancellous bone was cut using a 7 mm width osteotome and the anterior cortex was cut with use of a reciprocating saw (Figure 2). This osteotomy is similar to curved varus osteotomy, which has been use for the surgical treatment of femoral head osteonecrosis^[15].

After the planned intertrochanteric osteotomy, attachments of vastus muscles and the anterior capsule were detached from the intertrochanteric line of proximal segment to remove the proximal segment. And attachment of psoas was partially detached from the lesser trochanter.

On the inspection of the resected segment, no tumor showed a penetration into the joint or cortical invasion. Resected specimens were submitted for pathological evaluation.

The rest of the procedure was performed in the ordinary manner of cementless THA.

Three designs of implants were used; PINNACLE cup with Corail stem (DePuy, Saint-Priest, France) in 4 hips, PLASMACUP[®] SC acetabular component with BiCONTACT[®] stem (Aesculap, Tuttlingen, Germany) in 2 hips, and Bencox cup with Bencox stem (Corentec, Seoul, South Korea) in 1 hip. Third-generation ceramic articulation (BIOLOX Forte alumina head and liner; CeramTec, Plochingen, Germany) was used in 2 hips, and fourth-generation (BIOLOX Delta alumina head and liner; CeramTec) in 5 hips. The diameter of the femoral head was 28 mm in 1 hip, 32 mm in 5 hips, and 36 mm in 1 hip.

The final diagnoses by histological examination

were low-grade osteosarcoma, diffuse large B-cell lymphoma, liposclerosing myxofibroma, intraosseous lipoma, chondroblastoma, giant cell tumor, and focal intramedullary fibrosis (Table 1). Surgical margins were negative for the tumor in all patients.

Two patients with malignant tumors underwent a computed tomographic scan of the chest and whole body bone scan, which revealed no evidences of distant metastasis. The patient with lymphoma was treated with adjuvant chemotherapy. Patients were instructed to walk with partial weight bearing with the aid of two crutches for four weeks after surgery.

Routine follow-up visits were scheduled for six weeks, three, six, nine, twelve months, and six months thereafter. Patients who had not returned for regularly scheduled visits were contacted by telephone.

Clinical evaluation was performed with use of the Harris hip score (HHS)^[16], and the functional classification system of the International Society of Limb Salvage (ISOLS), which includes six functional parameters; pain, function, emotional acceptance, use of walking supports, walking ability, and gait. Each parameter is scored from 0 to 5 (a maximum score of 30)^[17].

The radiographic evaluation was done to confirm if there was the evidence of recurrence; a newly discovered osteolytic or osteosclerotic lesion on follow-up radiographs or MRI.

Fixations of the acetabular and femoral components^[18,19], ceramic wear^[20] and osteolysis^[21-23] were assessed on serial radiographs.

The design and protocol of this retrospective study were approved by the institutional review board in our hospital, which waived the informed consents.

RESULTS

Fracture of the greater trochanter occurred in one patient who was operated due to intraosseous lipoma. The fracture was detected on postoperative 6 wk radiographs. In this patient, the inner portion of the greater trochanter had been removed during the operation to achieve a wide resection and only a thin

Table 1 Patients demographics

Patient	Sex/age	Initial diagnosis on MRI	Final histologic diagnosis	Follow-up (yr)	ISOLS score
1	F/36	Giant cell tumor	Liposclerosing myxofibroma	6	30
2	F/38	Low-grade osteosarcoma	Low-grade osteosarcoma	6	29
3	F/64	Clear cell chondrosarcoma	Intraosseous lipoma	5	28
4	M/22	Chondroblastoma	Chondroblastoma	5	30
5	M/33	Giant cell tumor	Giant cell tumor	3	30
6	F/60	Breast cancer metastasis	Focal intramedullary fibrosis	3	28
7	M/41	Aneurysmal bone cyst	Lymphoma	Died at 10 mo	

F: Female; M: Male; MRI: Magnetic resonance imaging.

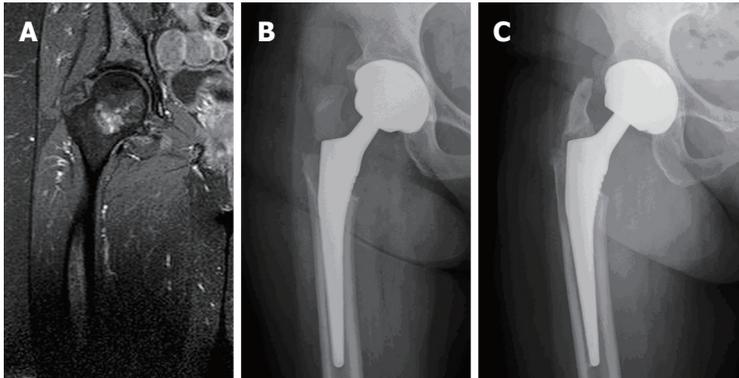


Figure 3 Radiographs of patient 3. A: Preoperative magnetic resonance imaging of a 64-year-old woman shows a high signal lesion confined to femoral head and neck; B: Postoperative radiograph at 6 wk after total hip arthroplasty with extensive excision at the intertrochanteric level shows an avulsion fracture of greater trochanter; C: Postoperative radiograph at 5 years after total hip arthroplasty with extensive excision at the intertrochanteric level shows no evidence of local recurrence and implant loosening or osteolysis.

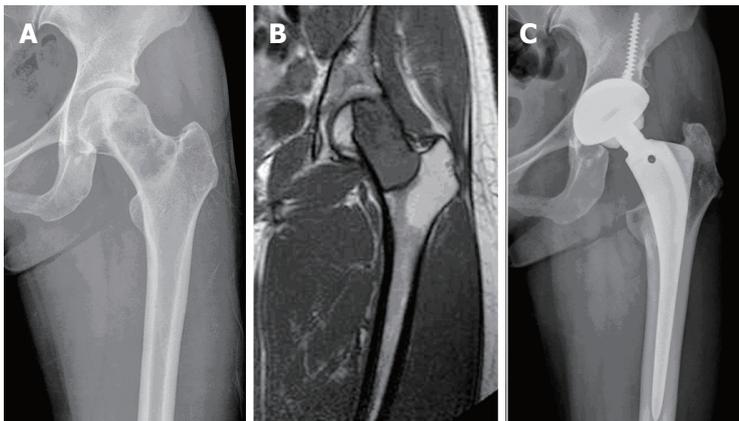


Figure 4 Radiographs of patient 1. A: Radiograph of a 36-year-old woman shows an osteolytic lesion confined to femoral head and neck; B: Preoperative magnetic resonance imaging shows a low signal intensity lesion with well-defined surrounding rim; C: Postoperative radiograph at 6 years after total hip arthroplasty with extensive excision at the intertrochanteric level shows no evidence of local recurrence and implant loosening or osteolysis.

cortical portion had been left. This patient had no history of trauma, and had little pain postoperatively. Thus, the fracture seemed to be an avulsion fracture. It healed completely with protected weight-bearing for 3 mo and an osseointegration of the prosthesis was achieved (Figure 3).

One patient with lymphoma recovered well and returned to his normal activity after the operation. The postoperative radiographs at 6 mo were uneventful. However, this patient died because of disseminated disease at the 10 mo postoperative.

The remaining 6 patients were followed-up for an average of 4.7 years (3 to 6 years). All patients returned to their daily activities and were walking with full weight bearing. At the last follow-up, the mean HHS was 98.0 points (range 96-100 points), and the mean ISOLS functional score was 29.2 points (range 28-30 points) (Table 1). During the follow-up there was no

evidence of local recurrence. At the latest follow-up, there were no radiographic signs of aseptic loosening, wear, or osteolysis (Figure 4).

DISCUSSION

The proximal femur is a common site for primary bone tumors and the most common site of metastatic tumors. Since the introduction of tumor prosthesis in 1980s, tumors in the femoral head and neck have been treated with extensive resection and reconstruction of the proximal femur. The femur is resected below the lesser trochanter and the greater trochanter is resected or osteomized. The reconstruction is consisted of a hemiarthroplasty with use of an endoprosthesis. Although modular system improved the endoprosthetic reconstruction^[14], there are several drawbacks in this procedure. The greater trochanter is osteotomized or

the abductors are transected through their tendinous attachments. If the greater trochanter is resected *en-bloc*, the remaining abductors are attached to the prosthesis. If a fragment of the greater trochanter remains, it is fixed to the prosthesis with a cable grip system.

However, problems have appeared after the use of cable grip. Silverton *et al*^[24] reviewed 68 trochanteric osteotomies, which were repaired with Dall-Miles cable grip system (Howmedica, Rutherford, NJ). Trochanteric nonunion occurred in 25%, with fraying and fragmentation of the cable. Among the 51 patients with trochanteric union, 35% also had signs of fraying and fragmentation. Osteolysis around the cable was seen in 10%. Metallosis at the inferior border of the acetabulum were seen in 12%^[24].

As the life expectancy of patients with bone tumors improves, endoprosthetic replacement of the proximal femur is not durable in young patients with low-grade tumor (IA/IB or benign)^[7]. Bernthal *et al*^[7] reviewed 86 proximal femoral replacements used for tumor reconstruction. Their study included 43 high-grade tumors (IIA/IIB), 20 low-grade tumors (IA/IB or benign), and 23 with metastatic disease. The 5-, 10-, and 20-year survival for IIA/IIB patients was 54%, 50%, and 44%, respectively; all patients with low-grade disease survived; the 5-year survival rate for patients with metastatic disease was 16%. The 5-, 10- and 20-year implant survivorships were 93%, 84%, and 56%, respectively. Although bipolar proximal femoral reconstruction proved a durable technique in patients with metastatic disease and high-grade disease, patients with low-grade disease outlived their implants^[7]. In this study, there was a suspicious solitary bone metastasis (patient 6), which was confirmed intramedullary fibrosis. Solitary bone metastasis is defined as a single skeletal metastasis with no tumor in any other part of the body including the primary cancer site or with a primary lesion in resectable status. Although there has been some debate on whether curative resection for a solitary bone metastasis leads to survival gain, most authors believed that patients with a solitary bone metastasis from several cancers live longer than those with multiple metastasis regardless of treatment modalities. Jung *et al*^[25] reported that patients who had wide resection for a solitary bone metastasis had a disease-specific survival rate of 100% at mean follow-up of 69 mo. Therefore, they suggested that patients with solitary bone lesion are candidates for aggressive surgical treatment with curative intent. In addition, durable reconstruction is needed to avoid revision surgery which may complicate future management for cancer.

Our study showed that trochanter/calcar preserving resection allows adequate surgical margins for tumors in femoral head and neck and reconstruction using conventional total hip prosthesis affords a satisfactory functional outcome without local recurrence or prosthetic loosening.

There were several limitations in our study. Our study was a retrospective review performed in a small number of cases. There was no control group of wide resection of the proximal femur and reconstruction using endo-prosthesis. However, the mean HHS (98 points) was satisfactory at last follow-up, which was comparable with that of primary THA^[26]. Our procedure is applicable on the condition that the lesion was confined to the femoral head and neck. Therefore, a careful evaluation of tumor extent using MRI is mandatory preoperatively.

Our results of trochanter/calcar preserving resection and reconstruction using conventional total hip prosthesis were satisfactory. We would recommend this procedure as a primary surgical treatment along with curettage and bone graft for tumors confined to the femoral head and neck, especially in young patients.

COMMENTS

Background

Tumors confined to the femoral head have been treated by curettage-bone graft or tumor prosthesis following an extensive resection of the proximal femur according to the suspected pathology. When using tumor prosthesis with high cost, an extensive resection of the proximal femur leads to sacrifice of the greater trochanter or the insertion of the abductor muscle. In this study, the authors presented a trochanter/calcar-preserving resection and conventional total hip prosthesis in tumors involving femoral head and neck, and evaluated the outcomes.

Research frontiers

This study contributes to presenting the surgical technique of total hip arthroplasty following trochanter/calcar-preserving resection in the selected patients.

Innovations and breakthroughs

In this study, trochanter/calcar-preserving resection was presented for patients with tumor confined to femoral head and neck. This technique does not require a sacrifice of greater trochanter which abductor muscles are inserted. This means that patients can preserve their abductor mechanism, even though surgery of proximal femur.

Applications

This study suggests that trochanter/calcar-preserving resection is useful for treatment in patients with tumor confined to femoral head and neck.

Terminology

Calcar: The dense, vertically oriented bone present in the posteroemial region of the femoral shaft inferior to the lesser trochanter of the femur.

Peer-review

The effort to reduce postoperative morbidity by preserving trochanter and calcar seemed to have yielded a good result.

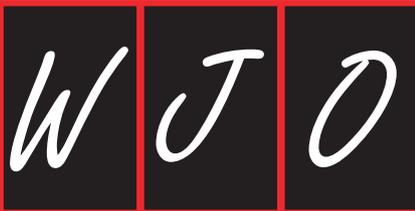
REFERENCES

- 1 **Unni K.** Dahlin's bone tumors. Philadelphia, PA: Lippincott-Raven, 1996: 72, 144, 250
- 2 **Ramappa AJ,** Lee FY, Tang P, Carlson JR, Gebhardt MC, Mankin HJ. Chondroblastoma of bone. *J Bone Joint Surg Am* 2000; **82-A:** 1140-1145 [PMID: 10954104]
- 3 **Springfield DS,** Capanna R, Gherlinzoni F, Picci P, Campanacci M. Chondroblastoma. A review of seventy cases. *J Bone Joint Surg Am*

- 1985; **67**: 748-755 [PMID: 3997927]
- 4 **Campanacci M**, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. *J Bone Joint Surg Am* 1987; **69**: 106-114 [PMID: 3805057]
 - 5 **Cho HS**, Park IH, Han I, Kang SC, Kim HS. Giant cell tumor of the femoral head and neck: result of intralesional curettage. *Arch Orthop Trauma Surg* 2010; **130**: 1329-1333 [PMID: 20020148 DOI: 10.1007/s00402-009-1026-2]
 - 6 **Ogilvie CM**, Wunder JS, Ferguson PC, Griffin AM, Bell RS. Functional outcome of endoprosthetic proximal femoral replacement. *Clin Orthop Relat Res* 2004; **(426)**: 44-48 [PMID: 15346050 DOI: 10.1097/01.blo.0000136840.67864.78]
 - 7 **Berenthal NM**, Schwartz AJ, Oakes DA, Kabo JM, Eckardt JJ. How long do endoprosthetic reconstructions for proximal femoral tumors last? *Clin Orthop Relat Res* 2010; **468**: 2867-2874 [PMID: 20440661 DOI: 10.1007/s11999-010-1369-6]
 - 8 **Finstein JL**, King JJ, Fox EJ, Ogilvie CM, Lackman RD. Bipolar proximal femoral replacement prostheses for musculoskeletal neoplasms. *Clin Orthop Relat Res* 2007; **459**: 66-75 [PMID: 17545760 DOI: 10.1097/BLO.0b013e31804f5474]
 - 9 **Jarit GJ**, Sathappan SS, Panchal A, Strauss E, Di Cesare PE. Fixation systems of greater trochanteric osteotomies: biomechanical and clinical outcomes. *J Am Acad Orthop Surg* 2007; **15**: 614-624 [PMID: 17916785 DOI: 10.5435/00124635-200710000-00006]
 - 10 **Simank HG**, Chatzipanagiotis C, Kaps HP. Complication rate following trochanteric osteotomy in total hip endoprosthesis. A retrospective study with failure analysis. *Z Orthop Ihre Grenzgeb* 1996; **134**: 457-464 [PMID: 8967148 DOI: 10.1055/s-2008-1037438]
 - 11 **Wieser K**, Zingg P, Dora C. Trochanteric osteotomy in primary and revision total hip arthroplasty: risk factors for non-union. *Arch Orthop Trauma Surg* 2012; **132**: 711-717 [PMID: 22228280 DOI: 10.1007/s00402-011-1457-4]
 - 12 **Glassman AH**. Complications of trochanteric osteotomy. *Orthop Clin North Am* 1992; **23**: 321-333 [PMID: 1570144]
 - 13 **Jeys LM**, Kulkarni A, Grimer RJ, Carter SR, Tillman RM, Abudu A. Endoprosthetic reconstruction for the treatment of musculoskeletal tumors of the appendicular skeleton and pelvis. *J Bone Joint Surg Am* 2008; **90**: 1265-1271 [PMID: 18519320 DOI: 10.2106/JBJS.F.01324]
 - 14 **Chandrasekar CR**, Grimer RJ, Carter SR, Tillman RM, Abudu A, Buckley L. Modular endoprosthetic replacement for tumours of the proximal femur. *J Bone Joint Surg Br* 2009; **91**: 108-112 [PMID: 19092014 DOI: 10.1302/0301-620X.91B1.20448]
 - 15 **Zhao G**, Yamamoto T, Ikemura S, Motomura G, Mawatari T, Nakashima Y, Iwamoto Y. Radiological outcome analysis of transtrochanteric curved varus osteotomy for osteonecrosis of the femoral head at a mean follow-up of 12.4 years. *J Bone Joint Surg Br* 2010; **92**: 781-786 [PMID: 20513873 DOI: 10.1302/0301-620X.92B6.23621]
 - 16 **Harris WH**. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. *J Bone Joint Surg Am* 1969; **51**: 737-755 [PMID: 5783851]
 - 17 **Enneking WF**, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res* 1993; **(286)**: 241-246 [PMID: 8425352 DOI: 10.1097/00003086-199301000-00035]
 - 18 **Engl CA**, Glassman AH, Suthers KE. The case for porous-coated hip implants. The femoral side. *Clin Orthop Relat Res* 1990; **(261)**: 63-81 [PMID: 2245564]
 - 19 **Latimer HA**, Lachiewicz PF. Porous-coated acetabular components with screw fixation. Five to ten-year results. *J Bone Joint Surg Am* 1996; **78**: 975-981 [PMID: 8698733]
 - 20 **Livermore J**, Ilstrup D, Morrey B. Effect of femoral head size on wear of the polyethylene acetabular component. *J Bone Joint Surg Am* 1990; **72**: 518-528 [PMID: 2324138]
 - 21 **Engl CA**, Hooten JP, Zettl-Schaffer KF, Ghaffarpour M, McGovern TF, Macalino GE, Zicat BA. Porous-coated total hip replacement. *Clin Orthop Relat Res* 1994; **(298)**: 89-96 [PMID: 8119001 DOI: 10.1097/00003086-199401000-00014]
 - 22 **DeLee JG**, Charnley J. Radiological demarcation of cemented sockets in total hip replacement. *Clin Orthop Relat Res* 1976; **(121)**: 20-32 [PMID: 991504 DOI: 10.1097/00003086-197611000-00003]
 - 23 **Gruen TA**, McNeice GM, Amstutz HC. "Modes of failure" of cemented stem-type femoral components: a radiographic analysis of loosening. *Clin Orthop Relat Res* 1979; **(141)**: 17-27 [PMID: 477100 DOI: 10.1097/00003086-197906000-00002]
 - 24 **Silverton CD**, Jacobs JJ, Rosenberg AG, Kull L, Conley A, Galante JO. Complications of a cable grip system. *J Arthroplasty* 1996; **11**: 400-404 [PMID: 8792246 DOI: 10.1016/S0883-5403(96)80029-5z]
 - 25 **Jung ST**, Ghert MA, Harrelson JM, Scully SP. Treatment of osseous metastases in patients with renal cell carcinoma. *Clin Orthop Relat Res* 2003; **(409)**: 223-231 [PMID: 12671506 DOI: 10.1097/01.blo.0000059580.08469.3e]
 - 26 **Lee YK**, Ha YC, Yoo JJ, Koo KH, Yoon KS, Kim HJ. Alumina-on-alumina total hip arthroplasty: a concise follow-up, at a minimum of ten years, of a previous report. *J Bone Joint Surg Am* 2010; **92**: 1715-1719 [PMID: 20660234 DOI: 10.2106/JBJS.I.01019]

P- Reviewer: Bicanic G, Jun Y S- Editor: Ji FF L- Editor: A
E- Editor: Wu HL





Extensor pollicis brevis tendon can hyperextend thumb interphalangeal joint in absence of extensor pollicis longus: Case report and review of the literature

Robert J Strauch, Carolyn B Strauch

Robert J Strauch, Department of Orthopaedic Surgery, Columbia University, New York, NY 10032, United States

Carolyn B Strauch, Dartmouth College, Hanover, NY 03755, United States

Author contributions: All authors contributed to the acquisition of data, writing, and revision of this manuscript.

Institutional review board statement: Attached-no formal IRB approval needed for case report.

Informed consent statement: The patient involved in this study gave his verbal consent to inclusion in this case report.

Conflict-of-interest statement: The authors have no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Robert J Strauch, MD, Professor of Orthopaedic Surgery, Department of Orthopaedic Surgery, Columbia University, 622 West 168th Street, PH11-1119, New York, NY 10032, United States. robertjstrauch@hotmail.com
Telephone: +1-212-3054272
Fax: +1-212-3054040

Received: January 30, 2016
Peer-review started: February 1, 2016
First decision: April 15, 2016
Revised: April 17, 2016
Accepted: May 7, 2016
Article in press: May 9, 2016

Published online: July 18, 2016

Abstract

We are reporting a case of extensor pollicis longus tendon rupture which did not require tendon transfer owing to the ability of the intact extensor pollicis brevis (EPB) to fully hyperextend the thumb interphalangeal joint. The thumb metacarpophalangeal joint was also able to be fully actively extended by the EPB. Previous anatomical studies have demonstrated that the insertional anatomy of the EPB tendon is highly variable and sometimes inserts onto the extensor hood and distal phalanx, which is likely the mechanism by which our patient was able to fully extend the thumb interphalangeal joint. Despite the potential for the EPB to extend the IP joint of the thumb, virtually all previously reported cases of extensor pollicis longus (EPL) tendon rupture had deficits of thumb IP extension requiring tendon transfer. This case highlights the potential ability of the EPB tendon to completely substitute for the function of the EPL tendon in providing thumb IP joint extension.

Key words: Extensor pollicis brevis; Extensor pollicis longus; Tendon rupture; Extensor pollicis longus tendon rupture

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The extensor pollicis brevis may be able to substitute for extensor pollicis longus (EPL) function in some patients when EPL has ruptured.

Strauch RJ, Strauch CB. Extensor pollicis brevis tendon can hyperextend thumb interphalangeal joint in absence of extensor

pollicis longus: Case report and review of the literature. *World J Orthop* 2016; 7(7): 448-451 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/448.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.448>

INTRODUCTION

Extensor pollicis longus (EPL) tendon rupture may occur spontaneously or following distal radius fracture, surgical fixation, or repetitive use^[1,2]. Virtually all reported cases of EPL tendon rupture have been treated by tendon transfer or tendon grafting in order to restore thumb interphalangeal joint extension. The extensor pollicis brevis (EPB) tendon is classically described as inserting upon the base of the thumb proximal phalanx providing thumb metacarpophalangeal joint extension. Several anatomic studies, however, have demonstrated the EPB insertional anatomy to be highly variable with potential insertions on the extensor hood as well as the distal phalanx (Table 1)^[3-8]. One study demonstrated that 21% of EPB tendons, when pulled on at the wrist level, would cause thumb IP joint extension in cadavers^[7]. It is therefore interesting that, to the best of our knowledge, there have been no reports of EPL rupture in which thumb MP and IP joint extension remains normal. We report a case of EPL tendon rupture in which normal thumb MP and IP motion was preserved most likely owing to the EPB inserting on the extensor hood and/or the distal phalanx.

CASE REPORT

A 64-year-old right handed man had sustained a right wrist scaphoid fracture in 1969 which went on to develop a scaphoid nonunion advanced collapsed deformity (SNAC wrist) with arthritic changes and a large bone spur from the dorsal scaphoid. Nevertheless, he had no wrist pain and the right wrist never bothered him enough to warrant treatment. Six weeks prior to presentation, he was reaching for something and felt a pop in his right wrist. His physician referred him for hand surgery evaluation. On physical examination his right wrist extended to 30 degrees and flexed to 30 degrees compared to 45 degrees and 70 degrees respectively on the left wrist. His right wrist had bony enlargement dorsally on the radial side, but was non-tender and there was no pain with motion. His EPL tendon was noted to be completely ruptured. However, his EPB tendon could visibly fully extend both the thumb MP and IP joints (Figures 1-3). His active thumb motion was 0-60 degrees at the MP joint and 15 degrees of hyperextension to 50 degrees of flexion at the IP joint. The only difference between the right and left thumbs was that when his hands were put flat on the table, he was unable to fully lift the right thumb up off the table compared to the left side (Figure 4 and Video core tip 1). X-rays of his right wrist revealed a SNAC wrist with



Figure 1 Patient demonstrating full thumb MP and IP extension using only extensor pollicis brevis tendon.



Figure 2 Examiner's finger pointing to extensor pollicis brevis tendon which is extending thumb at MP and IP joints.

a large bony osteophyte protruding dorsally from the scaphoid. The impression was that the EPL tendon had ruptured over the dorsal spike from the scaphoid as this was directly underlying the normal course of the EPL tendon and there was concern that his wrist extensors might also rupture over the bony spike. Therefore, a magnetic resonance imaging of the right wrist was obtained which revealed that the extensor carpi radialis longus (ECRL) tendon was 50% eroded over the dorsal spike of the scaphoid nonunion and that the EPL tendon had completely ruptured. After discussion with the patient, it was decided to perform a surgical procedure to debride the bone spike from the scaphoid nonunion that could potentially lead to rupture of his wrist extensor tendons, having already ruptured the EPL tendon. Since he had no pain in the wrist nor deficits of thumb IP joint extension we did not plan to perform any procedure to address the arthritis or the EPL rupture. At the time of surgery, which was performed under a regional anesthetic, the EPL tendon was seen to be completely ruptured with the proximal end retracted and the ECRL tendon was 50% eroded. The sharp spikes from the scaphoid nonunion were debrided and the capsule was closed over the scaphoid as a soft tissue interposition between the bone and the wrist

Table 1 Previous anatomic studies of extensor pollicis brevis insertional anatomy

Ref.	Type of study	# of hands	EPB insertion site
Stein ^[3]	Cadaver study	42 cadavers, 84 wrists dissected	No comment on insertional anatomy
Dawson <i>et al</i> ^[4]	Cadaver Study	16 hands of eight cadavers	56% inserted partly to the base of the first phalanx and partly to the extensor hood 25% inserted entirely on the base of the thumb proximal phalanx 19% inserted entirely onto the extensor hood 5% were absent - the Abductor pollicis longus tendon instead inserted partly to the extensor hood and partly to proximal phalanx Four out of the eight cadavers showed asymmetry of the EPB between right and left hands
Brunelliet <i>al</i> ^[5]	Cadaver study	52 hands	19% inserted onto proximal phalanx with most also having attachments to extensor hood 69% inserted into the extensor hood 8% inserted into the base of the distal phalanx 4% were absent
Kulshreshtha <i>et al</i> ^[6]	Cadaver study	44 hands 23 cadavers	25% inserted onto proximal phalanx 25% of tendons insert partly to the base of the proximal phalanx and partly to the extensor hood 2% of tendons inserted entirely into extensor hood 27% of tendons inserted partly to the base of the proximal phalanx and partly to the extensor hood, and from there, continuing further to the base of the distal phalanx with EPL 20% of tendons inserted into the extensor hood and, from there, continued further to the base of the distal phalanx with EPL The EPB was present in all hands, but anatomy of the EPB is variable on the left and right sides of 14 of the 21 paired hands
Alemohammad <i>et al</i> ^[7]	Clinical study and Cadaver study	90 cadaver wrists, and 143 patients undergoing Dequervain's release surgery	In the cadaver group - in 21% pulling on the EPB tendon produced thumb IP joint extension 79% inserted onto proximal phalanx 17% inserted onto distal phalanx 4% inserted onto extensor hood
Shigematsu <i>et al</i> ^[8]	Cadaver study	72 cadaver specimens, 144 hands	29% inserted entirely onto the extensor hood 22% inserted onto the base of the proximal phalanx 19% inserted partly onto the base of the proximal phalanx and partly into the extensor hood 9.0% inserted onto the base of the proximal phalanx and into the extensor hood, and then on the base of the distal phalanx, along with EPL 9.0% inserted onto the extensor hood, and then onto the base of the distal phalanx, along with the EPL 2% were completely absent with no accessory tendon 6% were absent but an accessory tendon inserted at the MP joint 4% had 2 EPB tendons - with variable insertions

EPB: Extensor pollicis brevis; EPL: Extensor pollicis longus.



Figure 3 Patient demonstrating thumb MP and IP flexion.



Figure 4 Extensor pollicis brevis tendon extending thumb (Video core tip 1).

extensor tendons. Post-operatively, he was immobilized for 10 d at which time the sutures were removed and

he resumed normal activities without pain. At 3 mo follow up he had no complaints of pain and was using

his hand and wrist normally.

DISCUSSION

To the best of our knowledge, virtually all previously reported cases of EPL tendon rupture have been associated with deficits of thumb interphalangeal joint extension. Anatomical dissections have shown the EPB tendon insertion to be highly variable with insertions on the thumb proximal phalanx as well as the extensor hood and the distal phalanx (Table 1). It is, therefore, reasonable to assume that a minority of EPL tendon ruptures may be clinically overlooked owing to the ability of the EPB tendon to fully extend the thumb interphalangeal joint. These cases may never come to the attention of physicians since, while the patients may experience a pop and temporary discomfort, their thumbs may continue to work fairly normally. The cases presenting to orthopedic and hand surgeons, therefore, may represent patients in whom the EPB tendon is unable to fully compensate for the function of the EPL tendon. This case report highlights the anatomical ability of the EPB tendon to fully substitute for the EPL tendon with respect to thumb interphalangeal joint extension. EPL tendon rupture may therefore be more common than is currently appreciated since cases such as these may never present for treatment.

COMMENTS

Case characteristics

A 64-year-old man with rupture of the extensor pollicis longus (EPL) tendon presenting with preserved ability to full extend his thumb at the interphalangeal and metacarpophalangeal joints.

Clinical diagnosis

The EPL tendon was noted to be ruptured both visibly, on examination, on magnetic resonance imaging (MRI) and at the time of surgical exploration, and yet the extensor pollicis brevis (EPB) tendon was able to fully extend the thumb at the IP and MP joints.

Differential diagnosis

The EPB tendon was clearly seen extending the thumb, likely due to its insertion on the extensor hood and/or distal phalanx.

Imaging diagnosis

MRI showed EPL tendon rupture.

Treatment

The prominent bony outgrowth that had caused the EPL rupture was surgically excised so it did not further erode the wrist extensor tendons.

Related reports

Virtually all previously reported series of EPL tendon rupture had deficits of IP thumb joint extension requiring surgery with tendon transfer or grafting. This case report highlights that tendon transfer may not always be required for EPL tendon rupture.

Term explanation

The EPB tendon and the EPL tendon both extend the thumb.

Experiences and lessons

There may be many patients with EPL tendon rupture who do not require tendon transfer due to the ability of the EPB to extend the thumb IP joint.

Peer-review

This is a concise and well written report which is of surgical interest. The video is a useful adjunct.

REFERENCES

- 1 **Kim CH.** Spontaneous rupture of the extensor pollicis longus tendon. *Arch Plast Surg* 2012; **39**: 680-682 [PMID: 23233902 DOI: 10.5999/aps.2012.39.6.68]
- 2 **Hu CH, Fufa D, Hsu CC, Lin YT, Lin CH.** Revisiting spontaneous rupture of the extensor pollicis longus tendon: eight cases without identifiable predisposing factor. *Hand (N Y)* 2015; **10**: 726-731 [PMID: 26568731 DOI: 10.1007/s11552-015-9746-y]
- 3 **Stein AH.** Variations of the tendons of insertion of the abductor pollicis longus and the extensor pollicis brevis. *Anat Rec* 1951; **110**: 49-55 [PMID: 14838330 DOI: 10.1002/ar.1091100106]
- 4 **Dawson S, Barton N.** Anatomical variations of the extensor pollicis brevis. *J Hand Surg Br* 1986; **11**: 378-381 [PMID: 3794479 DOI: 10.1016/0266-7681(86)90161-0]
- 5 **Brunelli GA, Brunelli GR.** Anatomy of the extensor pollicis brevis muscle. *J Hand Surg Br* 1992; **17**: 267-269 [PMID: 1624857 DOI: 10.1016/0266-7681(92)90112-F]
- 6 **Kulshreshtha R, Patel S, Arya AP, Hall S, Compson JP.** Variations of the extensor pollicis brevis tendon and its insertion: a study of 44 cadaveric hands. *J Hand Surg Eur Vol* 2007; **32**: 550-553 [PMID: 17950220 DOI: 10.1016/j.jhse.2007.04.013]
- 7 **Alemohammad AM, Yazaki N, Morris RP, Buford WL, Viegas SF.** Thumb interphalangeal joint extension by the extensor pollicis brevis: association with a subcompartment and de Quervain's disease. *J Hand Surg Am* 2009; **34**: 719-723 [PMID: 19345877 DOI: 10.1016/j.jhsa.2008.12.015]
- 8 **Shigematsu S, Shimizu H, Beppu M, Hirata K.** Anatomy of the extensor pollicis brevis associated with an extension mechanism of the thumb metacarpophalangeal joint. *Hand Surg* 2014; **19**: 171-179 [PMID: 24875499 DOI: 10.1142/S0218810414500166]

P- Reviewer: Musumeci G, Wharton R **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Wu HL



Hemorrhagic lumbar synovial facet cyst secondary to transforaminal epidural injection: A case report and review of the literature

Hossein Elgafy, Nicholas Peters, Justin E Lea, Robert M Wetzel

Hossein Elgafy, Nicholas Peters, Justin E Lea, Robert M Wetzel, Department of Orthopedic Surgery, University of Toledo Medical Center, Toledo, OH 43614, United States

Author contributions: All the authors contributed in outlining the manuscript, gathering the data, and writing the manuscript.

Institutional review board statement: This case report was exempt from the Institutional Review Board.

Informed consent statement: The patient involved in this study gave her written informed consent authorizing use and disclosure of her protected health information.

Conflict-of-interest statement: None of the authors have any financial or any other conflicts of interest that may bias the current study.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Hossein Elgafy, MD, MCH, FRCSEd, FRCSC, Department of Orthopaedic Surgery, University of Toledo Medical Center, 3065 Arlington Avenue, Toledo, OH 43614, United States. hossein.elgafy@utoledo.edu
Telephone: +1-419-3833515
Fax: +1-419-3836170

Received: January 25, 2016

Peer-review started: January 26, 2016

First decision: March 1, 2016

Revised: March 12, 2016

Accepted: May 10, 2016

Article in press: May 11, 2016

Published online: July 18, 2016

Abstract

A 64-year-old-female presented with progressive left foot weakness, low back and radicular pain after a left sided S1 transforaminal epidural steroid injection (ESI). Magnetic resonance imaging revealed left side L5-S1 large extradural heterogeneous mass with layering areas suggesting different stages of hematoma formation. Past medical history was significant for peripheral vascular disease and transient ischemic attacks, for which she took aspirin and clopidogrel (antiplatelet agent). These medications were discontinued one week prior to ESI. Although synovial cysts associated with facet arthropathy are common, hemorrhagic cyst is not. To the best of the authors' knowledge, this is the first reported case of symptomatic hemorrhagic lumbar facet synovial cyst following ESI on a patient taking antiplatelet medications.

Key words: Lumbar synovial cyst; Hemorrhage; Antiplatelet therapy; Epidural injection

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: With modern advances in magnetic resonance imaging studies, synovial cysts are seen with degenerative lumbar facet disease. A symptomatic synovial cyst usually presents with a gradual onset low back pain originating from facet arthropathy and radicular pain or neurogenic claudication due to nerve roots compression. Previous reports showed synovial cyst can present with a progressive radicular pain and weakness secondary to spontaneous hemorrhage into the cyst. To the authors' best knowledge, this is the first case report of iatrogenic hemorrhagic lumbar synovial cyst.

Elgafy H, Peters N, Lea JE, Wetzel RM. Hemorrhagic lumbar synovial facet cyst secondary to transforaminal epidural injection: A case report and review of the literature. *World J Orthop* 2016; 7(7): 452-457 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/452.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.452>

INTRODUCTION

Synovial cysts are relatively uncommon in the spine. Most cases are associated with facet joint arthritis and degenerative spondylolisthesis and occur most frequently at the L4-5 level. With modern advances in imaging studies, synovial cysts are becoming more evident as a common component of degenerative lumbar facet disease. Normally synovial cysts cause a gradual onset of symptoms that are typically indistinguishable from disc herniation or spinal stenosis^[1,2]. The purpose of the current study was to present a case of progressive radicular pain and weakness secondary to hemorrhage into a lumbar synovial cyst after transforaminal epidural injection. To the authors' best knowledge, this is the first case report of iatrogenic hemorrhagic lumbar synovial cyst.

CASE REPORT

A 64-year-old female patient was referred to the spine clinic with three weeks history of increasing low back pain radiating to the posterior aspect of the left thigh and leg. She also complained of a new-onset weakness in her left foot and difficulty with ambulation, which started after a left sided S1 transforaminal epidural steroid injection (ESI) that was performed by pain management physician. Past medical history was significant for hypertension, peripheral vascular disease and transient ischemic attacks, for which she took aspirin and clopidogrel (antiplatelet agent used in coronary artery disease, peripheral vascular disease, and cerebrovascular disease). These medications were discontinued one week prior to ESI. She had a several year history of L4-5 degenerative spondylolisthesis, multilevel disc degeneration and spinal stenosis and radiculopathy that had previously been effectively treated by ESI. Neurological examination revealed positive straight leg raise on the left side, diminished sensation over left L5, S1 nerve root dermatomes, and decreased motor strength (2/5) in extensor hallucis longus (EHL), plantar and dorsiflexion of the ankle on the left.

Plain radiographs showed severe multilevel disc degeneration and a grade I spondylolisthesis at L4-L5. Magnetic resonance imaging (MRI) showed an intraspinal extradural heterogeneous mass with decreased signal centrally within the T2 weighted sequences at L5-S1 on to the left side with displacement of the thecal sac to the

right (Figure 1). In STIR images, the lesion appeared heterogeneous but predominantly low in signal intensity and in T1 weighted images, it showed heterogeneous increased signal and layering areas suggesting different stages of hematoma formation (Figure 2). Blood work including erythrocyte sedimentation rate, C-reactive protein, uric acid level, coagulation and platelet studies were within normal limits.

The working diagnosis was a hemorrhagic synovial cyst with a differential diagnosis of sequestered disc, epidural metastasis and infection. Surgical treatment was indicated due to the increased back, leg pain, progressive left foot weakness and the severity of the spinal canal stenosis. The goal of the surgical treatment was decompression, excision of the lesion and L3-S1 instrumented fusion for the degenerative changes. The patient underwent L3-S1 midline sparing left side laminotomy, facetectomy and foraminotomy. The surgical microscope was used to identify the thecal sac above and below the lesion (Figure 3). Grossly, the lesion appeared to be a hematoma within a synovial cyst (Figure 4). This was impinging upon the transversing L5 and S1 nerve roots on the left side. The intraspinal cyst was then excised without sustaining any dural tear and L3-S1 instrumentation and posterolateral fusion performed for the degenerative lumbar spine (Figure 5). Postoperative histology assessment of the excised lesion confirmed the diagnosis of hematoma within a synovial cyst. At two weeks follow up, the patient's radicular pain had resolved. Additionally, she had improved strength in EHL, plantar and dorsiflexion of the left ankle. Two months post-operatively, the patient regained full strength, denied any radicular or back pain and remained pain free at the last follow up at two years.

DISCUSSION

The most common location of intraspinal synovial cyst is L4-5 motion segment as it is the most mobile level allowing for more degeneration of the facet joint. Symptomatic synovial cysts present with low back pain originating from facet arthropathy and radicular pain or neurogenic claudication due to nerve roots compression^[1-3]. The synovial cyst in the current case was located at L5-S1 rather than the most common L4-5 level with presenting symptoms of diminished sensation over left L5, S1 nerve root dermatomes and weakness of EHL, plantar and dorsiflexion of the left ankle. Acute exacerbation of the patient's symptoms was related to hemorrhage inside the cyst. There are previous reports of spontaneous hemorrhage without epidural injection. However, in the current case report, the timing of the presenting symptoms supports the thought that introduction of a needle into a pre-existing synovial cyst had led to subsequent intra-cystic hemorrhage and onset of radicular symptoms and weakness.

To the best of the authors' knowledge, there have been no published reports of hemorrhagic synovial

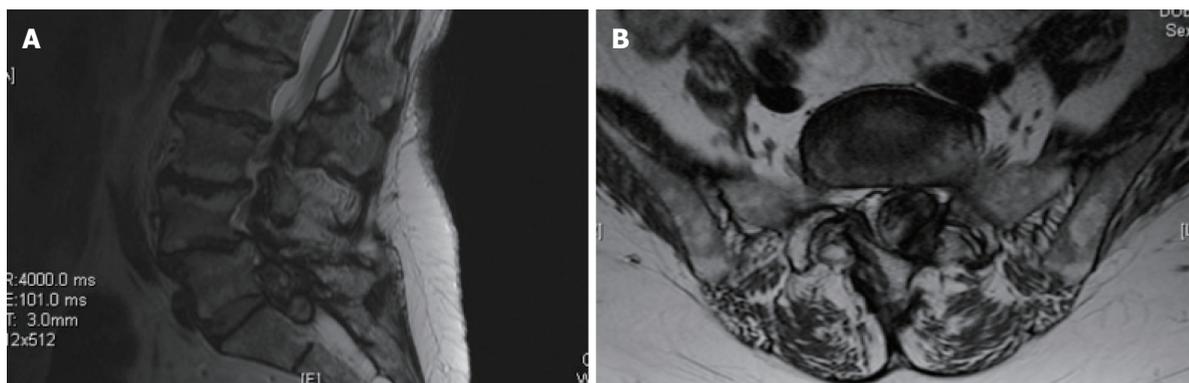


Figure 1 T2 weighted midsagittal (A) and axial (B) magnetic resonance imaging scan showed intraspinal extradural well delineated capsule containing a mixed signal intensity lesion on the left side at L5-S1 causing severe canal stenosis with displacement of the thecal sac to the right side.

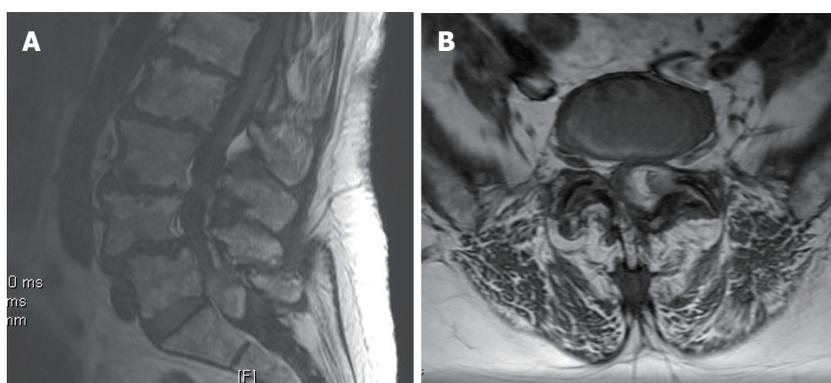


Figure 2 T1 weighted midsagittal (A) and axial (B) magnetic resonance imaging scan showed increased signal intensity with layering areas suggesting different stages of hematoma formation.

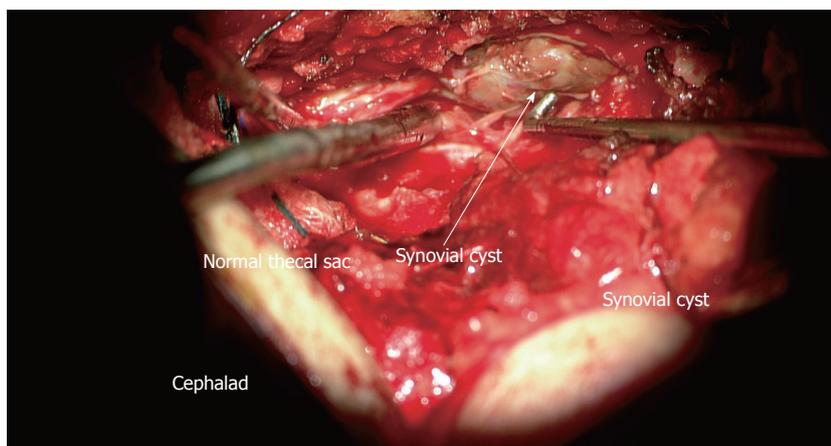


Figure 3 Intraoperative photograph taken by the surgical microscope showed a well-demarcated brown color cyst that was adherent to the thecal sac (arrow), a hematoma was found inside the cyst.

cyst following ESI on a patient taking anti-platelet medications. There have been several reported cases of symptomatic epidural hematoma following ESI. The literature reports an incidence of 1:150000 to 1:220000 for epidural hematoma following epidural anesthesia, however the incidence following transforaminal ESI is not quantified^[4-6].

MRI is the study of choice for diagnosing, however

their radiographic characteristics vary in the literature. Acutely, the cysts have been described as appearing hypo-intense on T1 weighted images while appearing hyper-intense on T2 weighted images. However, in the more commonly imaged subacute period, both the T1 and T2 signals may appear as hyper- or hypo-intense depending on the intracystic methemoglobin and hemosiderin content and the amount of calcification in the



Figure 4 Intraoperative photograph taken by the surgical microscope showed hematoma inside the cyst (arrow).

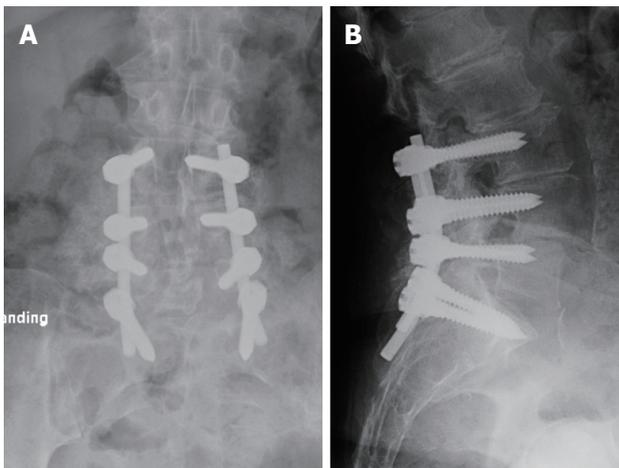


Figure 5 Postoperative anteroposterior and lateral roentgenograms showed L3-S1 instrumentation and posterolateral fusion.

cyst wall^[7,8]. The current case showed heterogeneous signals in the T2 and T1 weighted images with the signal predominantly decreased in T2 and increased in T1 with layering areas, which is consistent with the subacute interval between the onset of symptoms and the timing of the MRI.

The mainstay of surgical treatment is excision of the cyst and decompression of the involved neural structures. The role of fusion at the time of cyst excision and decompression remains controversial in patients displaying preoperative spondylolisthesis. The need for fusion is influenced by symptomatic preoperative instability as evidenced by dynamic radiographs or intraoperative instability that may be created by iatrogenic resection of spinal structures such as the pars interarticularis or the facet joints^[3]. Epstein *et al.*^[9] treated 80 patients with cyst excision and decompression without fusion. Thirty-five patients demonstrated preoperative Meyerding grade 1 spondylolisthesis. At two years follow up, 58% of patients who had no evidence of preoperative spondylolisthesis and 63% of patients with preoperative spondylolisthesis demonstrated good or excellent surgeon based outcomes. However, a moderate improvement was noted in only 2 of 8 SF-36 measures. Eleven patients had progression of listhesis

and two patients required surgical stabilization. Bydon *et al.*^[10] in a systemic review noted that 811 patients (84%) underwent decompressive excision alone while 155 patients (16%) had concomitant fusion. They reported that 6.2% of the patients required further operative intervention, the majority of which were for instability and mechanical back pain. Additionally, they found that cyst recurrence occurred in 1.8% of patients who underwent decompression alone while no cases of recurrent cysts were found in patients who underwent fusion.

Surgical excision and decompression of lumbar cysts are not without complication. Banning *et al.*^[11] reported dural tear in 3 of 29 (9%) patients who underwent laminotomy and cyst excision. Larger cysts or cysts that are calcified due to chronicity can become adherent to the dura making their dissection more complex. Other reported complications include spinal nerve injury, epidural hematoma, seroma, and cyst recurrence^[12].

Definitive diagnosis is typically reached by histologic examination. Hemorrhagic synovial cysts are characterized by hematologic, fibrous and endothelial elements. Hemosiderin or blood may be seen depending on the acuity and size of the hemorrhage^[7,8,13]. The patient's pathology in the current study demonstrated blood elements, fibrin and synovium consistent with the diagnosis of hemorrhagic synovial cyst.

Anticoagulation has been implicated in the pathogenesis of hemorrhagic cysts. Nourbakhsh *et al.*^[8] as well as Eck and Triantafyllou, reported cases of radiculopathy secondary to hemorrhagic cyst formation in patients taking warfarin. Both patients required surgical decompression and experienced postoperative resolution of their symptoms^[8,13]. Spontaneous spinal epidural hematoma in patients taking anti-platelet medication has been reported in the literature^[14-16]. Much research has been directed at spinal anesthesia in patients taking anti-thrombotic or anti-platelet medications. There is no current data that suggest low dose aspirin is associated with increased risk of epidural hematoma in the setting of a normal platelet count. Current guidelines set forth by the American Society of Regional Anesthesia and Pain Medicine call for cessation of clopidogrel 7 d prior to a neuraxial procedure such as

ESI^[17,18]. The patient presented in the current report had discontinued the anti-platelet medication in a manner consistent with published guidelines, and coagulation and platelet studies were within normal limits before the transforaminal ESI. However, the timing of the presenting symptoms as well as the radiographic and histologic findings support the thought that introduction of a needle into a pre-existing synovial cyst had led to subsequent intra-cystic hemorrhage and onset of radicular symptoms and weakness.

COMMENTS

Case characteristics

A 64-year-old female presented with progressive left foot weakness, low back and radicular pain after a left sided S1 transforaminal epidural steroid injection (ESI). Past medical history was significant for peripheral vascular disease and transient ischemic attacks, for which she took aspirin and clopidogrel (antiplatelet agent). These medications were discontinued one week prior to ESI.

Clinical diagnosis

Neurological examination revealed positive straight leg raise on the left side, diminished sensation over left L5, S1 nerve root dermatomes, and decreased motor strength (2/5) in extensor hallucis longus, plantar and dorsiflexion of the ankle on the left.

Differential diagnosis

Sequestered disc, epidural metastasis and infection.

Laboratory diagnosis

Blood work including erythrocyte sedimentation rate, C-reactive protein, uric acid level, coagulation and platelet studies were within normal limits.

Imaging diagnosis

Plain radiographs showed severe multilevel disc degeneration and a grade I spondylolisthesis at L4-L5. Magnetic resonance imaging showed an intraspinal extradural heterogeneous mass with decreased signal centrally within the T2 weighted sequences at L5-S1 on to the left side with displacement of the thecal sac to the right.

Treatment

The patient underwent midline sparing left side laminotomy, facetectomy and foraminotomy. The intraspinal cyst was then excised under the surgical microscope.

Related reports

To the best of the authors' knowledge, this is the first reported case of symptomatic hemorrhagic lumbar facet synovial cyst following ESI on a patient taking anti-platelet medications.

Term explanation

Intraspinal extradural synovial cysts are associated with facet joint arthritis and degenerative spondylolisthesis and occur most frequently at the L4-5 level.

Experiences and lessons

Patients taking anticoagulation or anti-platelet medication should be informed that even if they stop their medication at the time recommended, there is still a possibility of intraspinal bleeding that may result in progressive neurological deficit after transforaminal ESI. Furthermore, transforaminal ESI may be avoided at the level, where a synovial cyst presents, to mitigate such a complication.

Peer-review

The authors present an interesting case of a hemorrhagic synovial cyst

developing after a transforaminal epidural steroid injection.

REFERENCES

- 1 **Wilby MJ**, Fraser RD, Vernon-Roberts B, Moore RJ. The prevalence and pathogenesis of synovial cysts within the ligamentum flavum in patients with lumbar spinal stenosis and radiculopathy. *Spine (Phila Pa 1976)* 2009; **34**: 2518-2524 [PMID: 19927101 DOI: 10.1097/BRS.0b013e3181b22bd0]
- 2 **Shah RV**, Lutz GE. Lumbar intraspinal synovial cysts: conservative management and review of the world's literature. *Spine J* 2003; **3**: 479-488 [PMID: 14609693 DOI: 10.1016/S1529-9430(03)00148-7]
- 3 **Sabo RA**, Tracy PT, Weinger JM. A series of 60 juxtafacet cysts: clinical presentation, the role of spinal instability, and treatment. *J Neurosurg* 1996; **85**: 560-565 [PMID: 8814156 DOI: 10.3171/jns.1996.85.4.0560]
- 4 **Stoll A**, Sanchez M. Epidural hematoma after epidural block: implications for its use in pain management. *Surg Neurol* 2002; **57**: 235-240 [PMID: 12173390 DOI: 10.1016/S0090-3019(02)00639-0]
- 5 **Xu R**, Bydon M, Gokaslan ZL, Wolinsky JP, Witham TF, Bydon A. Epidural steroid injection resulting in epidural hematoma in a patient despite strict adherence to anticoagulation guidelines. *J Neurosurg Spine* 2009; **11**: 358-364 [PMID: 19769520 DOI: 10.3171/2009.3.SPINE0916]
- 6 **Shanthanna H**, Park J. Acute epidural haematoma following epidural steroid injection in a patient with spinal stenosis. *Anaesthesia* 2011; **66**: 837-839 [PMID: 21790519 DOI: 10.1111/j.1365-2044.2011.06770.x]
- 7 **Ramieri A**, Domenicucci M, Seferi A, Paolini S, Petrozza V, Delfini R. Lumbar hemorrhagic synovial cysts: diagnosis, pathogenesis, and treatment. Report of 3 cases. *Surg Neurol* 2006; **65**: 385-390, discussion 390 [PMID: 16531204 DOI: 10.1016/j.surneu.2005.07.073]
- 8 **Nourbakhsh A**, Garges KJ. Lumbar synovial joint hematoma in a patient on anticoagulation treatment. *Spine (Phila Pa 1976)* 2007; **32**: E300-E302 [PMID: 17450063 DOI: 10.1097/01.brs.0000261410.07412.83]
- 9 **Epstein NE**. Lumbar laminectomy for the resection of synovial cysts and coexisting lumbar spinal stenosis or degenerative spondylolisthesis: an outcome study. *Spine (Phila Pa 1976)* 2004; **29**: 1049-1055; discussion 1056 [PMID: 15105680 DOI: 10.1097/0007632-200405010-00018]
- 10 **Bydon A**, Xu R, Parker SL, McGirt MJ, Bydon M, Gokaslan ZL, Witham TF. Recurrent back and leg pain and cyst reformation after surgical resection of spinal synovial cysts: systematic review of reported postoperative outcomes. *Spine J* 2010; **10**: 820-826 [PMID: 20488765 DOI: 10.1016/j.spinee.2010.04.010]
- 11 **Banning CS**, Thorell WE, Leibrock LG. Patient outcome after resection of lumbar juxtafacet cysts. *Spine (Phila Pa 1976)* 2001; **26**: 969-972 [PMID: 11317123 DOI: 10.1097/00007632-200104150-00024]
- 12 **Lyons MK**, Atkinson JL, Wharen RE, Deen HG, Zimmerman RS, Lemens SM. Surgical evaluation and management of lumbar synovial cysts: the Mayo Clinic experience. *J Neurosurg* 2000; **93**: 53-57 [PMID: 10879758]
- 13 **Eck JC**, Triantafyllou SJ. Hemorrhagic lumbar synovial facet cyst secondary to anticoagulation therapy. *Spine J* 2005; **5**: 451-453 [PMID: 15996615 DOI: 10.1016/j.spinee.2005.01.005]
- 14 **Wang L**, Liu G, Subramaniam S, Wong TA, Kumar N. Spontaneous spinal epidural haematoma after antiplatelet treatment: a report of two cases. *J Orthop Surg (Hong Kong)* 2012; **20**: 386-390 [PMID: 23255653]
- 15 **Sung JH**, Hong JT, Son BC, Lee SW. Clopidogrel-induced spontaneous spinal epidural hematoma. *J Korean Med Sci* 2007; **22**: 577-579 [PMID: 17596676 DOI: 10.3346/jkms.2007.22.3.577]
- 16 **Lim SH**, Hong BY, Cho YR, Kim HS, Lee JI, Kim HW, Ko YJ. Relapsed spontaneous spinal epidural hematoma associated with aspirin and clopidogrel. *Neurol Sci* 2011; **32**: 687-689 [PMID: 21384274 DOI: 10.1007/s10072-011-0508-5]
- 17 **Vandermeulen E**. Regional anaesthesia and anticoagulation. *Best Pract Res Clin Anaesthesiol* 2010; **24**: 121-131 [PMID: 20402175]

DOI: 10.1016/j.bpa.2009.09.004]

- 18 **Horlocker TT**, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, Brown DL, Heit JA, Mulroy MF, Rosenquist RW, Tryba M, Yuan CS. Regional anesthesia in the patient receiving

antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med* 2010; **35**: 64-101 [PMID: 20052816 DOI: 10.1097/AAP.0b013e3181c15c70]

P- Reviewer: Bydon A, Peng BG, Recnik G, Sharma G, Tokuhashi Y
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Wu HL



Operative stabilization of the remaining mobile segment in ankylosed cervical spine in systemic onset - juvenile idiopathic arthritis: A case report

Lovro Suhodolčan, Marko Mihelak, Janez Breclj, Rok Vengust

Lovro Suhodolčan, Janez Breclj, Rok Vengust, Department of Orthopaedic Surgery, University Medical Centre Ljubljana, 1000 Ljubljana, Slovenia

Marko Mihelak, Department of Orthopaedic Surgery, General Hospital Celje, 3000 Celje, Slovenia

Author contributions: Suhodolčan L gathered data of presented manuscript, made interpretation of data, wrote the majority of manuscript, processed figures, predominantly involved in designing and drafting manuscript; Mihelak M gathered literature regarding manuscript, participated in presenting data and designing manuscript body; Breclj J made clinical examination and follow-up visits, made all surgical interventions on patient's lower limbs previous to surgical intervention presented in this manuscript, made substantial contribution in designing manuscript, participated coordination and helped to draft the manuscript; Vengust R made the surgical intervention presented in this manuscript, has been involved in drafting the manuscript and revising it critically for important intellectual content.

Institutional review board statement: This case report was exempt from the Institutional Review Board standards at University of Ljubljana, Slovenia.

Informed consent statement: Patient gave informed consent.

Conflict-of-interest statement: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Lovro Suhodolčan, MD, PhD, Consultant Orthopaedic Surgeon of the Department of Orthopaedic Surgery, University Medical Centre Ljubljana, Zaloška 9, 1000 Ljubljana, Slovenia. lovro.suhodolcan@kclj.si
Telephone: +386-1-5224174
Fax: +386-1-5222474

Received: January 21, 2016
Peer-review started: January 22, 2016
First decision: March 24, 2016
Revised: April 4, 2016
Accepted: May 31, 2016
Article in press: June 2, 2016
Published online: July 18, 2016

Abstract

We describe a case of a 19-year-old young man with oligoarthritis type of juvenile idiopathic arthritis, who presented with several month duration of lower neck pain and progressive muscular weakness of all four limbs. X-rays of the cervical spine demonstrated spontaneous apophyseal joint fusion from the occipital condyle to C6 and from C7 to Th2 with marked instability between C6 and C7. Surgical intervention began with anterolateral approach to the cervical spine performing decompression, insertion of cage and anterior vertebral plate and screws, followed by posterior approach and fixation. Care was taken to restore sagittal balance. The condition was successfully operatively managed with multisegmental, both column fixation and fusion, resulting in pain cessation and resolution of myelopathy. Postoperatively, minor swallowing difficulties were noted, which ceased after three days. Patient was able to move around in a wheelchair on the sixth postoperative day. Stiff neck collar was advised for three months postoperatively with neck pain slowly decreasing in the course of first postoperative month.

On the follow-up visit six months after the surgery patient exhibited no signs of spastic tetraparesis, X-rays of the cervical spine revealed solid bony fusion at single mobile segment C6-C7. He was able to gaze horizontally while sitting in a wheelchair. Signs of myelopathy with stiff neck and single movable segment raised concerns about intubation, but were successfully managed using awake fiber-optic intubation. Avoidance of tracheostomy enabled us to perform an anterolateral approach without increasing the risk of wound infection. Regarding surgical procedure, the same principles are obeyed as in management of fracture in ankylosing spondylitis or Mb. Forestrier.

Key words: Juvenile idiopathic arthritis; Cervical ankylosis; Spastic tetraparesis; Multilevel both column fixation; Unstable cervical segment

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The spontaneous cervical apophyseal joint fusion is rare and only seen in juvenile type rheumatoid arthritis, where spontaneous fusions of more than three cervical segments are extremely uncommon. We present a patient with fusion of all but C6-C7 level. The single mobile segment became highly unstable, producing mechanical pain with symptoms of myelopathy. Prior to the surgery, awake fiber-optic intubation was used. Surgical intervention began with the anterolateral approach to the cervical spine performing decompression, insertion of cage and anterior vertebral plate and screws, followed by posterior approach and fixation. Care was taken to restore sagittal balance.

Suhodolčan L, Mihelak M, Brecej J, Vengust R. Operative stabilization of the remaining mobile segment in ankylosed cervical spine in systemic onset - juvenile idiopathic arthritis: A case report. *World J Orthop* 2016; 7(7): 458-462 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i7/458.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i7.458>

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is an exclusion diagnosis that applies to any arthritis of unknown origin, persisting for more than 6 wk and with the onset before the age of 16 years^[1]. Patients who belong to oligoarthritis type of JIA are characterized by an asymmetric arthritis affecting mainly large joints of an early onset (before 6 years of age), a female predilection, a high frequency of positive antinuclear antibodies, a high risk for developing chronic iridocyclitis and consistent HLA associations, which is typical of children and is not seen in adults^[2,3].

Recent advances in medical treatment enable more favorable prognosis, but rapid progressing cases may result in severe complications such as joint deformities,

Table 1 Characteristics of first-reported case of long-segment cervical fusion^[5]

Patient characteristics
27-yr-old female
JIA for 10 yr
Symptoms
Posterior neck pain
Progressive weakness
Paresthesia and dysesthesia below the C7 dermatome
Imaging
Spontaneous apophyseal joint fusion from the occipital condyle to C6
Instability at C6/C7 level - only mobile segment
Problems during procedure
Contracture of temporo-mandibular joint
Endotracheal intubation not feasible due to stiff neck
Tracheostomy needed
Severe osteoporosis noted
Approach/type of fixation
Posterior approach
Decompressive subtotal laminectomy
Interspinous process wiring with titanium-braded cable and addition of integrated bone graft at C6/7 level
Results
Pathologic reflexes disappeared
Well established bone graft incorporation 6 mo post-op
Conclusion
First-reported case of long-segment cervical fusion, may be related with rapid progression of the disease

JIA: Juvenile idiopathic arthritis.

joint ankylosis, osteoporosis and decreased bone mass. The common clinical manifestation of spinal involvement is the instability of upper cervical spine. The spontaneous cervical apophyseal joint fusion is rare and only seen in juvenile type rheumatoid arthritis, where one-or two level fusions occur in up to 41 percents of cases^[4]. On the other hand, spontaneous fusions of more than three cervical segments are reported to be extremely rare (Table 1)^[5].

We report a case of spontaneous cervical ankylosis from the occiput to C6 and from C7 to Th2 with sub-adjacent instability at C6-C7 level and neurological deficit in patient with JIA, which has been operatively stabilized.

CASE REPORT

A 19-year-old young man with oligoarthritis type of JIA presented with several month duration of lower neck pain and progressive muscular weakness of all four limbs. He had been treated previously for major contractures of the hip, knee and ankles. The valgus of the both knees was corrected with a temporary hemiepiphysiodesis at the age of 12. At the age of 15 an elongation of Achilles tendon and the knee flexors were performed. Total hip replacement was performed at the age of 15 on the left side and a year later on the right side. He has been partly wheelchair-bound for 3 years before admission due to extensive contractures of hips, knees and ankles. But he was able to walk short distances with the help of crutches. At the age of 12,



Figure 1 Plain X-rays at the age of 12 of cervical spine showed loss of lordosis and posterior fusion from C2 to C6 joints.

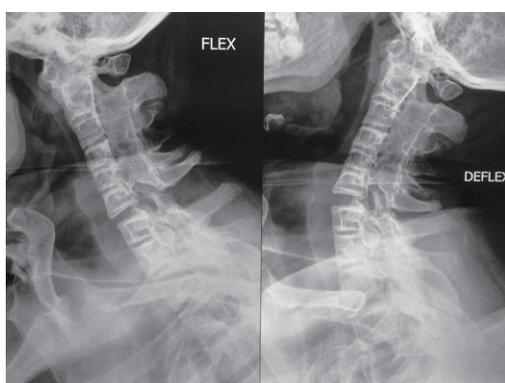


Figure 2 Bending films on admission showed spontaneous apophyseal joint fusion from the occipital condyle to C6 and from C7 to Th2 with marked instability between C6 and C7.

pain in the cervical spine occurred for the first time, followed by occasional mild pain episodes. The patient had been treated with methotrexate, steroids and antihypertensive therapy.

Clinical examination revealed markedly limited mobility of cervical spine with rotations being completely blocked. Flexion and extension resulted in significant pain in lower cervical spine. Patient was unable to walk independently, with signs of spastic tetraparesis.

Loss of lordosis and sclerotic changes of the facet joints in cervical plain X-rays had been present 7 years before admission (Figure 1). X-rays of the cervical spine on the day of the admission demonstrated spontaneous apophyseal joint fusion from the occipital condyle to C6 and from C7 to Th2. Bending films showed marked instability between C6 and C7 (Figure 2). There were no radiographic abnormalities of thoracolumbar spine. Computerized tomography/angiography confirmed apophyseal fusion of the entire cervical spine except for the C6-C7 level, where the left vertebral artery was dominant. Spinal canal was narrowed at C6-C7 due to posteriorly protruding spondylophytes. MRI revealed C6-C7 disc degeneration with spinal canal stenosis but no signal changes in spinal cord.

The patient underwent surgical intervention because

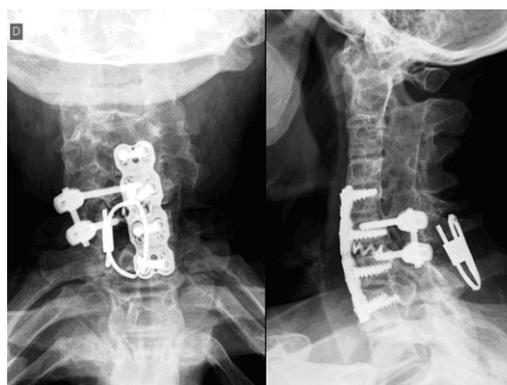


Figure 3 Post-operative plain X-rays.

of progredient spastic tetraparesis. Surgery was started after awake fiberoptic intubation. We began the procedure using anterolateral approach to the spine, where discectomy and osteophyte removal was performed, followed by the insertion of cage filled with bone substitute at the C6-C7 level. Vertebral bodies C5, C6 were fixed to C7, Th1 using anterior vertebral plate and screws (Figure 3).

Later on, the patient was turned prone, and cervical spine was accessed using the posterior approach. Posterior fixation was obtained using unilateral pedicular screws combined with an interspinous wire. Pedicular screws were inserted on the right side only, due to very small caliber vertebral artery ipsilaterally. Bone substitute was placed to the decorticated C6-C7 apophyseal joints. Care was taken to fix the spine in a position, which would enable the patient to gaze horizontally in a sitting position (Figure 4).

After the surgery patient had mild swallowing difficulties, which ceased after three days. He was able to move around in a wheelchair on the sixth postoperative day. Stiff neck collar was advised for three months postoperatively with neck pain slowly decreasing in the course of the first postoperative month. On the follow-up visit six months after the surgery the patient exhibited no signs of myelopathy, X-rays of the cervical spine revealed solid bony fusion at C6-C7 level. He was able to gaze horizontally while sitting in a wheelchair.

DISCUSSION

JIA of the spine was once believed to be a benign disease process. Many studies have shown, however, that the spectrum of joint erosion, deformity, ensuing neurological deficit, and underlying pathologic mechanisms warrant concern, especially in cervical spine^[6-8]. The most common pathologic condition is a spontaneous posterior cervical fusion seen in the late stage of the disease. Fusion usually occurs in one or two segments without clinical consequences^[5]. Apart from this, our patient presented with fusion of all but one level of cervical spine. The single mobile segment became highly

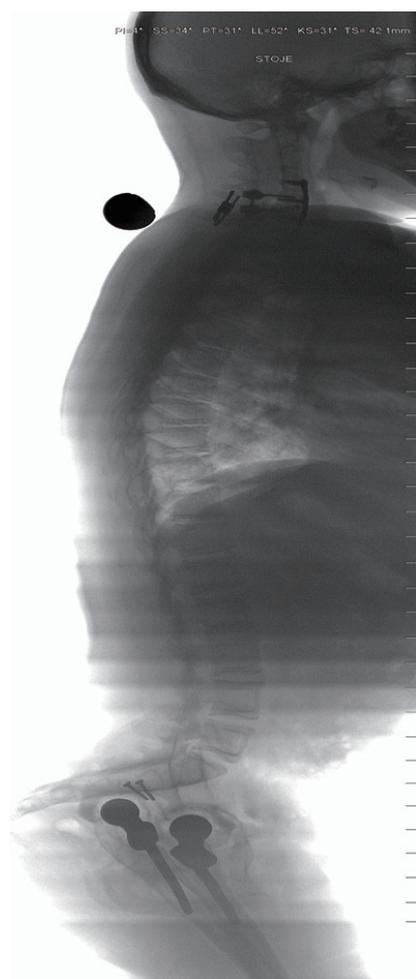


Figure 4 Post-operative scan; showing restored sagittal alignment.

unstable over time and produced mechanical pain, which along with symptoms of myelopathy forced the patient to consult a physician. The clinical course of progressive stiffness with escalating localized pain is unique in childhood and only resembles the pseudoarthrosis in ankylosing spondylitis in adults^[9,10].

Regarding surgical procedure the same principles were obeyed as in management of fracture in ankylosing spondylitis or Mb. Forestier^[11,12]. Multilevel both column fixation was performed employing combined anterolateral and posterior approach. Signs of myelopathy with stiff neck and single movable segment raised concerns about intubation, but were successfully managed using awake fiber-optic intubation. Avoidance of tracheostomy enabled us to perform the anterolateral approach without increasing the risk of wound infection. To the best of our knowledge, this is the first-reported case of multisegmental cervical ankylosis in JIA, operatively managed with combined anterior and posterior spinal interbody fusion.

As with other cases of stiff cervical spine, special care has to be taken to achieve proper sagittal alignment^[13]. With careful preoperative planning fixation should be achieved, which suits patient best in terms of

optimal gaze.

We present a JIA patient with a multisegmental spontaneous fusion of cervical spine. The one segment remaining mobile became overtly instable causing mechanical neck pain and progressive spastic tetraparesis. The condition was operatively managed with multisegmental, both column fixation and fusion, resulting in pain cessation and resolution of myelopathy symptoms six months postoperatively.

COMMENTS

Case characteristics

A 19-year-old young man with oligoarthritis type of juvenile idiopathic arthritis presented with several month duration of lower neck pain and progressive muscular weakness of all four limbs.

Clinical diagnosis

Clinical examination revealed markedly limited mobility of cervical spine with rotations being completely blocked. Flexion and extension resulted in significant pain in lower cervical spine. Patient was unable to walk independently, with signs of spastic tetraparesis.

Differential diagnosis

Ankylosing spondylitis, Mb. Forestier, Diffuse idiopathic skeletal hyperostosis.

Laboratory diagnosis

All labs were within normal limits.

Imaging diagnosis

X-rays of the cervical spine on the day of the admission demonstrated spontaneous apophyseal joint fusion from the occipital condyle to C6 and from C7 to Th2. Flexion and extension X-rays showed wide apophyseal joint space between C6 and C7, suggesting instability and excessive mobility. Computerized tomography confirmed ankylosis at the C0-C1 level.

Pathological diagnosis

Juvenile idiopathic arthritis.

Treatment

Surgical intervention with the anterolateral approach to the cervical spine, performing decompression, insertion of cage and anterior vertebral plate and screws, followed by posterior approach and fixation.

Related reports

Rapid progressing cases of juvenile idiopathic arthritis may result in severe complications such as joint deformities, joint ankylosis, osteoporosis and decreased bone mass. The common clinical manifestation of spinal involvement is the instability of upper cervical spine. The spontaneous cervical apophyseal joint fusion is rare and only seen in juvenile type rheumatoid arthritis, where one- or two level fusions occur in up to 41 percents of cases. Spontaneous fusions of more than three cervical segments are reported to be extremely rare.

Term explanation

Juvenile idiopathic arthritis (JIA) is an exclusion diagnosis that applies to any arthritis of unknown origin, persisting for more than 6 wk and with the onset before the age of 16 years.

Experiences and lessons

The single mobile segment of multisegmental cervical ankylosis in JIA that produces mechanical pain and neurologic deficit should be operatively managed. Awake fiber-optic intubation can be used prior to the surgery to overcome concerns of stiff neck. Avoidance of tracheostomy enables combined anterior

and posterior spinal interbody fusion without increasing the risk of wound infection. Care should be taken to restore sagittal balance.

Peer-review

It is a very good paper.

REFERENCES

- 1 **Prakken B**, Albani S, Martini A. Juvenile idiopathic arthritis. *Lancet* 2011; **377**: 2138-2149 [PMID: 21684384 DOI: 10.1016/S0140-6736(11)60244-4]
- 2 **Petty RE**, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, He X, Maldonado-Cocco J, Orozco-Alcala J, Prieur AM, Suarez-Almazor ME, Woo P. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004; **31**: 390-392 [PMID: 14760812]
- 3 **Martini A**, Lovell DJ. Juvenile idiopathic arthritis: state of the art and future perspectives. *Ann Rheum Dis* 2010; **69**: 1260-1263 [PMID: 20525835 DOI: 10.1136/ard.2010.133033]
- 4 **Laiho K**, Savolainen A, Kautiainen H, Kekki P, Kauppi M. The cervical spine in juvenile chronic arthritis. *Spine J* 2002; **2**: 89-94 [PMID: 14588266 DOI: 10.1016/S1529-9430(02)00151-1]
- 5 **Kim H**, Yang DH, Kim SH, Shin YS, Ahn YH, Yoon SH, Cho KG, Cho H. Long-segment Spontaneous Cervical Arthrodesis in Juvenile Rheumatoid Arthritis. *Kor J Spine* 2007; **4**: 157-160
- 6 **Cabot A**, Becker A. The cervical spine in rheumatoid arthritis. *Clin Orthop Relat Res* 1978; **(131)**: 130-140 [PMID: 657609 DOI: 10.1097/00003086-197803000-00017]
- 7 **Hensinger RN**, DeVito PD, Ragsdale CG. Changes in the cervical spine in juvenile rheumatoid arthritis. *J Bone Joint Surg Am* 1986; **68**: 189-198 [PMID: 3944157]
- 8 **Shen FH**, Samartzis D, Jenis LG, An HS. Rheumatoid arthritis: evaluation and surgical management of the cervical spine. *Spine J* 2004; **4**: 689-700 [PMID: 15541704 DOI: 10.1016/j.spinee.2004.05.001]
- 9 **Peh WC**, Luk KD. Pseudoarthrosis in ankylosing spondylitis. *Ann Rheum Dis* 1994; **53**: 206-210 [PMID: 8154942 DOI: 10.1136/ard.53.3.206]
- 10 **Kanefield DG**, Mullins BP, Freehafer AA, Furey JG, Horenstein S, Chamberlin WB. Destructive lesions of the spine in rheumatoid ankylosing spondylitis. *J Bone Joint Surg Am* 1969; **51**: 1369-1375 [PMID: 5823200]
- 11 **Olerud C**, Frost A, Bring J. Spinal fractures in patients with ankylosing spondylitis. *Eur Spine J* 1996; **5**: 51-55 [PMID: 8689417 DOI: 10.1007/BF00307827]
- 12 **Chaudhary SB**, Hullinger H, Vives MJ. Management of acute spinal fractures in ankylosing spondylitis. *ISRN Rheumatol* 2011; **2011**: 150484 [PMID: 22389792 DOI: 10.5402/2011/150484]
- 13 **Kim DH**, Betz RR, Huhn SI, Newton PO. Surgery of the pediatric spine. *Thieme medical publishers* 2008: 375-379 [DOI: 10.1055/b-002-72236]

P- Reviewer: Firstenberg MS, Jiang B, Kettering K, Najafi M, Peteiro J, Ueda H **S- Editor:** Qiu S **L- Editor:** A **E- Editor:** Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 August 18; 7(8): 463-518



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Morais Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*

**Denmark**

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*

**Egypt**

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*

**Finland**

Hannu T Aro, *Turku*

**France**

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*

**Germany**

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*

**Greece**

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*

**Hungary**

Andor Sebestyén, *Pécs*

**India**

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*

**Iran**

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*

**Israel**

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*

**Italy**

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*

**Japan**

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*

**Jordan**

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*

**Malaysia**

Areezo Eshraghi, *Kuala Lumpur*

**Netherlands**

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*

**New Zealand**

Gary J Hooper, *Christchurch*

**Poland**

Agnieszka Tomaszewska, *Gdańsk*

**Saudi Arabia**

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*

**Serbia**

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

W

J

O

EDITORIAL

- 463 Lateral elbow tendinopathy: Evidence of physiotherapy management
Dimitrios S

ORIGINAL ARTICLE**Basic Study**

- 467 Antibiotic-loaded phosphatidylcholine inhibits staphylococcal bone infection
Jennings JA, Beenken KE, Skinner RA, Meeker DG, Smeltzer MS, Haggard WO, Troxel KS
- 475 Using simulation to train orthopaedic trainees in non-technical skills: A pilot study
Heaton SR, Little Z, Akhtar K, Ramachandran M, Lee J

Retrospective Cohort Study

- 481 Criteria for level 1 and level 2 trauma codes: Are pelvic ring injuries undertriaged?
Haws BE, Wuertzer S, Raffield L, Lenchik L, Miller AN

Retrospective Study

- 487 Femoro Patella Violla patellofemoral arthroplasty: An independent assessment of outcomes at minimum 2-year follow-up
Halai M, Ker A, Anthony I, Holt G, Jones B, Blyth M

- 494 Condensing osteitis of the clavicle in children
Andreacchio A, Marengo L, Canavese F

Observational Study

- 501 Four corner fusion using a multidirectional angular stable locking plate
Chaudhry T, Spiteri M, Power D, Brewster M
- 507 Validation of the functional rating index for the assessment of athletes with neck pain
Naghdi S, Nakhostin Ansari N, ShamsSalehi S, Feise RJ, Entezary E

CASE REPORT

- 513 Slacklining and stroke: A rehabilitation case study considering balance and lower limb weakness
Gabel CP, Rando N, Melloh M

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Ettore Vulcano, MD, Doctor, Department of Foot and Ankle, Institute for Foot and Ankle Reconstruction, Baltimore, MD 21202, United States

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central, and Scopus.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Huan-Liang Wu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Xin Kong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL OFFICE
 Jin-Lei Wang, Director

Xiu-Xia Song, Vice Director
World Journal of Orthopedics
 Room 903, Building D, Ocean International Center,
 No. 62 Dongsihuan Zhonglu, Chaoyang District,
 Beijing 100025, China
 Telephone: +86-10-59080039
 Fax: +86-10-85381893
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-223-8242
 Fax: +1-925-223-8243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.wjnet.com/esps/helpdesk.aspx>
<http://www.wjnet.com>

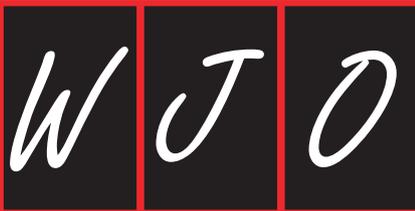
PUBLICATION DATE
 August 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.wjnet.com/esps/>



Lateral elbow tendinopathy: Evidence of physiotherapy management

Stasinopoulos Dimitrios

Stasinopoulos Dimitrios, Physiotherapy Program, Department Health Sciences, School of Sciences, European University of Cyprus, 1516 Nicosia, Cyprus

Author contributions: Dimitrios S solely contributed to this manuscript.

Conflict-of-interest statement: The author has no conflict of interests.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Stasinopoulos Dimitrios, PhD, Physiotherapy Program, Department Health Sciences, School of Sciences, European University of Cyprus, 6, Diogenes Str. Engomi, 1516 Nicosia, Cyprus. d.stassinopoulos@euc.ac.cy
Telephone: +357-22-713044

Received: February 16, 2016

Peer-review started: February 19, 2016

First decision: March 25, 2016

Revised: April 20, 2016

Accepted: June 14, 2016

Article in press: June 16, 2016

Published online: August 18, 2016

Abstract

Lateral elbow tendinopathy (LET) is a common musculo-skeletal/sports injury. A plethora of physiotherapy techniques has been proposed in the management of LET. The exercise programme is the most common treatment in the management of LET. The optimal

protocol of exercise programme is still unknown. The effectiveness of the exercise programme is low when it is applied as monotherapy. Therefore, exercise programme is combined with other physiotherapy modalities such as soft tissue techniques, external support, acupuncture, manual therapy and electrotherapy, in the treatment of LET. Future research is needed to determine which treatment strategy combined with exercise programme will provide the best results in LET rehabilitation.

Key words: Tennis elbow; Isometric exercises; Physical therapy; Electrotherapeutic modalities; Eccentric training; Stretching; Physical modalities; Manipulation; Lateral epicondylitis; Lateral elbow tendinopathy

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: An effective treatment approach in the management of lateral elbow tendinopathy (LET) is an exercise programme. Exercise programme improves patients' symptoms but the ideal exercise protocol for the management of LET is still under investigation. Exercise programme as a sole treatment approach does not respond positively in many patients with LET. Thus, physiotherapists combine exercise programme with other physiotherapy techniques like electrotherapy, manual therapy, taping/bracing and acupuncture. Research to determine which treatment approach combined with exercise programme will provide the best results in the management of LET is needed.

Dimitrios S. Lateral elbow tendinopathy: Evidence of physiotherapy management. *World J Orthop* 2016; 7(8): 463-466
Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/463.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.463>

Lateral epicondylalgia, lateral epicondylitis, tennis elbow and/or lateral epicondylitis are inappropriate

clinical diagnostic terms due to pathophysiological, anatomical aetiological and factors^[1]. Therefore, lateral elbow tendinopathy (LET) is the most appropriate clinical diagnostic term. LET is related to sport or arm work pain disorder. It is defined as a cause of pain in the lateral epicondyle^[2] that failed healing tendon response rather than inflammatory or may be degenerative^[3]. LET is characterized by the absence of inflammatory cells, glycosaminoglycans and proteoglycans, disorganized and immature collagen vascular hyperplasia, the increased presence of fibroblasts^[4]. The most commonly affected structure is the origin of the extensor carpi radialis brevis^[4]. LET is common between 30 and 60 years of age, the disorder appears to be more severe and of longer duration in females^[3,5] and the most commonly affected arm is the dominant arm^[2,6].

The main complaints of LET patients are decreased function and pain^[2,3]. Both symptoms affect daily activities. Pain can be reproduced with one of the following ways: (1) palpation on the facet of the lateral epicondyle; (2) with the elbow in extension, resisted wrist extension and/or resisted middle-finger extension; and (3) gripping activities^[2,3,7]. The Patient-Rated Tennis Elbow Evaluation questionnaire has been translated and culturally adapted into German^[8], Italian^[9], Swedish^[10] and Greek^[11] and provides a quick, standardized, and easy quantitative description of functional disability and pain in LET patients^[8].

Although the diagnosis of LET is not difficult, the proper management is unknown. Physiotherapy is usually recommended for the management of LET^[7,12]. A plethora of physiotherapy techniques, electrotherapeutic and non-electrotherapeutic modalities, has been recommended for the management of LET^[2,3,7,12-15]. The aim of these treatments is the same, improving function and reducing pain, but the theoretical mechanism of action of these treatments is different. Therefore, more research is needed to find out the most effective treatment approach in LET patients since this variety of treatment techniques suggests that the most proper treatment technique is not known^[2,3].

One of the most common physiotherapy treatments for LET is a supervised or in clinic exercise programme^[2,3,7,12,14]. Malliaras *et al*^[16] concluded that instead of eccentric loading in lower limb tendinopathy, clinicians should consider eccentric-concentric loading alongside. A Heavy Slow Resistance (HSR) program is recommended in the management of lower limb tendinopathy for young active people^[17,18]. There are not similar studies for the upper limb. A similar loading program may be beneficial for the management of LET^[2,3,7,12,14].

Alfredson *et al*^[19] were first proposed the eccentric training of the injured tendon, the most commonly used conservative technique in the management of tendinopathy. Systematic review^[20,21] and RCT^[22] favor eccentric over other types of contractions in the management of LET, but using only eccentric training of the injured tendon is not effective treatment

approach for some patients with upper and lower limb tendinopathies^[23]. Thus, eccentric contractions of the injured tendon is combined with stretching exercises, especially static, of the injured tendon in the rehabilitation of tendinopathies as it was proposed by Stanish *et al*^[24]. The patients in the Stanish exercise program, perform a five-steps program. A general, whole-body warm-up exercise is the first step. Static stretching exercises for the injured tendon are carried out in the second step. Next, the eccentric training is carried out once daily (3 sets of 10 repetitions) for six weeks and after six weeks, the patients are carried out three times per week for six more weeks 3 sets of 10 repetitions. Discomfort, or pain, is experienced in the last set of 10 repetitions. The eccentric training is described in detailed in the Stanish *et al*^[24] article. Every treatment ends with the same stretching exercise as described in the second step. Ice on the «injured» tendon for about 5-10 min after the program is used by the patients. There are not studies to support the efficacy of the Stanish exercise protocol in LET patients.

It was stated by Martinez-Silvestrini *et al*^[25] that isometric contraction, which would be more beneficial than eccentric contraction in LET because it is often related to forceful grip activities. Recently, isometric training has been recommended to decrease and manage the pain of tendon increasing the strength at the angle of contraction without producing inflammatory signs^[26]. Forty five second isometric mid-range quadriceps exercise reduced the pain of patellar tendon for 45 min post exercise^[26]. The dosage of isometric contractions in the present is based on clinical experience^[26-28] and their effect on LET pain requires further research. Therefore, it was hypothesized that the simultaneous use of these two kinds of contractions (isotonic and isometric) and static stretching exercises will further enhance the analgesic effect of contractions in the treatment of LET, increasing the arm function^[29]. However, the optimal protocol of exercise training needs to be investigated although the supervised exercise program is more effective than the home exercise program^[30].

Exercise program is rarely delivered as a treatment in isolation in the management of LET^[2]. An exercise program is usually combined with a range of physical therapy modalities. Furthermore, many manual therapies for the management of LET have been advocated, but the evidence to support the effectiveness of manual therapy in the management of tendinopathy is minimal^[31]. The most common manipulative techniques for the treatment of LET are Cyriax manual technique, Mulligan manipulation, mobilization of the neck, manipulation of the wrist and radial neural mobilization are^[32]. Manual therapy may increase grip strength and reduce pain immediately following treatment, but the evidence of any long-term clinical effects for manual therapy alone is insufficient^[2,3,7,12,14].

Treatment focusing on trigger points reduces pain and improves function in LET patients^[33]. A solid

conclusion will be formulated when high and large quality RCTs are carried out^[2]. Myofascial pain management methods such as deep transverse friction, low level laser, dry needling, etc., should also be evaluated^[2]. The additional effect of myofascial methods, it would be interesting to determine on exercise program or other treatment methods used in management of LET^[2,12,14].

Electrotherapeutic modalities such as low level laser, transcutaneous electrical nerve stimulation, extracorporeal shockwave therapy, pulsed electromagnetic field therapy therapeutic, ultrasound and iontophoresis are commonly used to manage LET^[7,12,14,15,29,34]. Well-conducted trials are needed to determine the effectiveness of the above reported modalities in the management of LET. It is believed that the exercise training alone in the rehabilitation of LET is less effective therapeutic approach than the combination of exercise training with electrotherapeutic modality/ies^[2,3,7,12,14,15].

External support such as bracing/taping is recommended for the management of LET^[2]. The evidence for the effectiveness of bracing/taping in the improvement of function and reduction of pain is conflicted^[35]. There was no compelling evidence that any one kind of bracing/any type of taping is superior to another in the short term, or that adding an external support to another treatment provides any additional benefit^[7,12].

At the end of the treatment and/or at the short-term follow up acupuncture is an effective LET treatment^[2,7,12]. The pathology of tendinopathy does not reverse using acupuncture, but it improves the signs of LET, reducing pain and increasing the function, but it^[36]. To draw definite conclusions about the effectiveness of acupuncture, more research with well - designed clinical trials are needed.

Finally, the most promising treatment approach in the management of LET is the exercise training but more research is needed to investigate the optimal protocol of exercise training. When the exercise program is applied as part of the rehabilitation process its effectiveness is higher than it is applied as monotherapy^[2,7,12,37]. More research to find out which treatment approach combined with exercises is needed to provide the best results in the management of LET.

REFERENCES

- 1 **Stasinopoulos D**, Johnson MI. 'Lateral elbow tendinopathy' is the most appropriate diagnostic term for the condition commonly referred-to as lateral epicondylitis. *Med Hypotheses* 2006; **67**: 1400-1402 [PMID: 16843614]
- 2 **Bisset LM**, Vicenzino B. Physiotherapy management of lateral epicondylalgia. *J Physiother* 2015; **61**: 174-181 [PMID: 26361816 DOI: 10.1016/j.jphys.2015.07.015]
- 3 **Coombes BK**, Bisset L, Vicenzino B. Management of Lateral Elbow Tendinopathy: One Size Does Not Fit All. *J Orthop Sports Phys Ther* 2015; **45**: 938-949 [PMID: 26381484 DOI: 10.2519/jospt.2015.5841]
- 4 **Kraushaar BS**, Nirschl RP. Tendinosis of the elbow (tennis elbow). Clinical features and findings of histological, immunohistochemical, and electron microscopy studies. *J Bone Joint Surg Am* 1999; **81**: 259-278 [PMID: 10073590]
- 5 **Waugh EJ**, Jaglal SB, Davis AM, Tomlinson G, Verrier MC. Factors associated with prognosis of lateral epicondylitis after 8 weeks of physical therapy. *Arch Phys Med Rehabil* 2004; **85**: 308-318 [PMID: 14966719 DOI: 10.1016/S0003-9993(03)00480-5]
- 6 **Vicenzino B**, Collins D, Wright A. The initial effects of a cervical spine manipulative physiotherapy treatment on the pain and dysfunction of lateral epicondylalgia. *Pain* 1996; **68**: 69-74 [PMID: 9252000]
- 7 **Sims SE**, Miller K, Elfar JC, Hammert WC. Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials. *Hand (N Y)* 2014; **9**: 419-446 [PMID: 25414603 DOI: 10.1007/s11552-014-9642-x]
- 8 **Rompe JD**, Overend TJ, MacDermid JC. Validation of the Patient-Rated Tennis Elbow Evaluation questionnaire. *J Hand Ther* 2007; **20**: 3-10 [DOI: 10.1197/j.jht.2006.10.003]
- 9 **Cacchio A**, Necozone S, MacDermid JC. Cross-cultural adaptation and measurement properties of the Italian Version of the Patient-Rated Tennis Elbow Evaluation (PRTEE) questionnaire. *Phys Ther* 2012; **2**: 1036-1045 [DOI: 10.2522/ptj.20110398]
- 10 **Nilsson P**, Baigi A, Marklund B, Månsson J. Cross-cultural adaptation and determination of the reliability and validity of PRTEE-S (Patientskattad Utvärdering av Tennisarmbåge), a questionnaire for patients with lateral epicondylalgia, in a Swedish population. *BMC Musculoskelet Disord* 2008; **9**: 79 [PMID: 18534009 DOI: 10.1186/1471-2474-9-79]
- 11 **Stasinopoulos D**, Papadopoulos C, Antoniadou M, Nardi L. Greek adaptation and validation of the Patient-Rated Tennis Elbow Evaluation (PRTEE). *J Hand Ther* 2015; **28**: 286-290; quiz 291 [PMID: 26003013 DOI: 10.1016/j.jht.2014.12.005]
- 12 **Weber C**, Thai V, Neuheuser K, Groover K, Christ O. Efficacy of physical therapy for the treatment of lateral epicondylitis: a meta-analysis. *BMC Musculoskelet Disord* 2015; **16**: 223 [PMID: 26303397 DOI: 10.1186/s12891-015-0665-4]
- 13 **Bisset L**, Paungmali A, Vicenzino B, Beller E. A systematic review and meta-analysis of clinical trials on physical interventions for lateral epicondylalgia. *Br J Sports Med* 2005; **39**: 411-422; discussion 411-422 [PMID: 15976161 DOI: 10.1136/bjsm.2004.016170]
- 14 **Menta R**, Randhawa K, Côté P, Wong JJ, Yu H, Sutton D, Varatharajan S, Southerst D, D'Angelo K, Cox J, Brown C, Dion S, Mior S, Stupar M, Shearer HM, Lindsay GM, Jacobs C, Taylor-Vaisey A. The effectiveness of exercise for the management of musculoskeletal disorders and injuries of the elbow, forearm, wrist, and hand: a systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMA) collaboration. *J Manipulative Physiol Ther* 2015; **38**: 507-520 [PMID: 26130104 DOI: 10.1016/j.jmpt.2015.06.002]
- 15 **Dingemans R**, Randsdorp M, Koes BW, Huisstede BM. Evidence for the effectiveness of electrophysical modalities for treatment of medial and lateral epicondylitis: a systematic review. *Br J Sports Med* 2014; **48**: 957-965 [PMID: 23335238 DOI: 10.1136/bjsports-2012-091513]
- 16 **Malliaras P**, Barton CJ, Reeves ND, Langberg H. Achilles and patellar tendinopathy loading programmes : a systematic review comparing clinical outcomes and identifying potential mechanisms for effectiveness. *Sports Med* 2013; **43**: 267-286 [PMID: 23494258 DOI: 10.1007/s40279-013-0019-z]
- 17 **Beyer R**, Kongsgaard M, Hougs Kjaer B, Øhlenschläger T, Kjaer M, Magnusson SP. Heavy Slow Resistance Versus Eccentric Training as Treatment for Achilles Tendinopathy: A Randomized Controlled Trial. *Am J Sports Med* 2015; **43**: 1704-1711 [PMID: 26018970 DOI: 10.1177/0363546515584760]
- 18 **Kongsgaard M**, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, Kaldau NC, Kjaer M, Magnusson SP. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports* 2009; **19**: 790-802 [PMID: 19793213 DOI: 10.1111/j.1600-0838.2009.00949.x]
- 19 **Alfredson H**, Pietilä T, Jonsson P, Lorentzon R. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. *Am J Sports Med* 1998; **26**: 360-366 [PMID: 9617396]

- 20 **Raman J**, MacDermid JC, Grewal R. Effectiveness of different methods of resistance exercises in lateral epicondylitis--a systematic review. *J Hand Ther* 2012; **25**: 5-25; quiz 26 [PMID: 22075055 DOI: 10.1016/j.jht.2011.09.001]
- 21 **Cullinane FL**, Boocock MG, Trevelyan FC. Is eccentric exercise an effective treatment for lateral epicondylitis? A systematic review. *Clin Rehabil* 2014; **28**: 3-19 [PMID: 23881334 DOI: 10.1177/0269215513491974]
- 22 **Peterson M**, Butler S, Eriksson M, Svärdsudd K. A randomized controlled trial of eccentric vs. concentric graded exercise in chronic tennis elbow (lateral elbow tendinopathy). *Clin Rehabil* 2014; **28**: 862-872 [PMID: 24634444 DOI: 10.1177/0269215514527595]
- 23 **Cannell LJ**, Taunton JE, Clement DB, Smith C, Khan KM. A randomised clinical trial of the efficacy of drop squats or leg extension/leg curl exercises to treat clinically diagnosed jumper's knee in athletes: pilot study. *Br J Sports Med* 2001; **35**: 60-64 [PMID: 11157465 DOI: 10.1136/bjism.35.1.60]
- 24 **Stanish WD**, Rubinovich RM, Curwin S. Eccentric exercise in chronic tendinitis. *Clin Orthop Relat Res* 1986; (**208**): 65-68 [PMID: 3720143]
- 25 **Martinez-Silvestrini JA**, Newcomer KL, Gay RE, Schaefer MP, Kortebein P, Arendt KW. Chronic lateral epicondylitis: comparative effectiveness of a home exercise program including stretching alone versus stretching supplemented with eccentric or concentric strengthening. *J Hand Ther* 2005; **18**: 411-419; quiz 420 [PMID: 16271688 DOI: 10.1197/j.jht.2005.07.007]
- 26 **Rio E**, Kidgell D, Purdam C, Gaida J, Moseley GL, Pearce AJ, Cook J. Isometric exercise induces analgesia and reduces inhibition in patellar tendinopathy. *Br J Sports Med* 2015; **49**: 1277-1283 [PMID: 25979840 DOI: 10.1136/bjsports-2014-094386]
- 27 **Stasinopoulos D**. The Effectiveness of Isometric Contractions Combined with Eccentric Contractions and Stretching Exercises on Pain and Disability in Lateral Elbow Tendinopathy. A Case Report. *J Nov Physiother* 2015; **5**: 238 [DOI: 10.4172/2165-7025.1000238]
- 28 **Malliaras P**, Cook J, Purdam C, Rio E. Patellar Tendinopathy: Clinical Diagnosis, Load Management, and Advice for Challenging Case Presentations. *J Orthop Sports Phys Ther* 2015; **45**: 887-898 [PMID: 26390269 DOI: 10.2519/jospt.2015.5987]
- 29 **Dimitrios S**. Exercise for tendinopathy. *World J Methodol* 2015; **5**: 51-54 [PMID: 26140271 DOI: 10.5662/wjm.v5.i2.51]
- 30 **Stasinopoulos D**, Stasinopoulos I, Pantelis M, Stasinopoulou K. Comparison of effects of a home exercise programme and a supervised exercise programme for the management of lateral elbow tendinopathy. *Br J Sports Med* 2010; **44**: 579-583 [PMID: 19887440 DOI: 10.1136/bjism.2008.049759]
- 31 **Bennett A**, Watson T, Simmonds J. The Efficacy of The Use Of Manual Therapy In The Management Of Tendinopathy: A Systematic Review. *BJSM* 2014; **48**: A11-A12 [DOI: 10.1136/bjsports-2014-094114.17]
- 32 **Hoogvliet P**, Randsdorp MS, Dingemans R, Koes BW, Huisstede BM. Does effectiveness of exercise therapy and mobilisation techniques offer guidance for the treatment of lateral and medial epicondylitis? A systematic review. *Br J Sports Med* 2013; **47**: 1112-1119 [PMID: 23709519 DOI: 10.1136/bjsports-2012-091990]
- 33 **Shmushkevich Y**, Kalichman L. Myofascial pain in lateral epicondylalgia: a review. *J Bodyw Mov Ther* 2013; **17**: 434-439 [PMID: 24139000 DOI: 10.1016/j.jbmt.2013.02.003]
- 34 **Thiele S**, Thiele R, Gerdsmeyer L. Lateral epicondylitis: This is still a main indication for extracorporeal shockwave therapy. *Int J Surg* 2015; **24**: 165-170 [PMID: 26455532 DOI: 10.1016/j.ijsu.2015.09.034]
- 35 **Shamsoddini A**, Hollisaz MT. Effects of taping on pain, grip strength and wrist extension force in patients with tennis elbow. *Trauma Mon* 2013; **18**: 71-74 [PMID: 24350156 DOI: 10.5812/traumamon.12450]
- 36 **Speed C**. Acupuncture's role in tendinopathy: new possibilities. *Acupunct Med* 2015; **33**: 7-8 [PMID: 25576594 DOI: 10.1136/acupmed-2014-010746]
- 37 **Stasinopoulos D**, Stasinopoulou K, Johnson MI. An exercise programme for the management of lateral elbow tendinopathy. *Br J Sports Med* 2005; **39**: 944-947 [PMID: 16306504 DOI: 10.1136/bjism.2005.019836]

P- Reviewer: Fukuchi RK, Hernandez-Sanchez S **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Wu HL



Basic Study

Antibiotic-loaded phosphatidylcholine inhibits staphylococcal bone infection

Jessica Amber Jennings, Karen E Beenken, Robert A Skinner, Daniel G Meeker, Mark S Smeltzer, Warren O Haggard, Karen S Troxel

Jessica Amber Jennings, Warren O Haggard, Department of Biomedical Engineering, University of Memphis, Memphis, TN 38152, United States

Karen E Beenken, Daniel G Meeker, Mark S Smeltzer, Department of Microbiology and Immunology, University of Arkansas Medical Sciences, Little Rock, AR 72205, United States

Robert A Skinner, Jamesport, NY 11947, United States

Karen S Troxel, Zimmer Biomet, Warsaw, IN 46581, United States

Author contributions: Jennings JA planned and performed the majority of experiments and analyzed the data; Beenken KE and Smeltzer MS planned and assisted with animal experiments; Skinner RA and Meeker DG performed surgical procedures; Skinner RA assisted with histological analysis; Haggard WO and Troxel KS assisted with materials formulation and planning experiments.

Supported by Institutional support from Biomet, LLC.

Institutional animal care and use committee statement: Animal studies were approved by the Institutional Review Board at the University of Arkansas for Medical Sciences (IACUC protocol #3540) and followed the IACUC guidelines.

Animal care and use statement: Study protocols were approved by the University of Arkansas for Medical Sciences IACUC and all appropriate measures were taken to minimize pain and discomfort.

Conflict-of-interest statement: Studies were funded and by Biomet, LLC. Karen S Troxel, PhD, is an employee of Zimmer Biomet.

Data sharing statement: Technical appendix, statistical analysis, and dataset available from the corresponding author at jjennings@memphis.edu.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Jessica Amber Jennings, PhD, Assistant Professor, Department of Biomedical Engineering, University of Memphis, 330 Engineering Technology Building, Memphis, TN 38152, United States. jjennings@memphis.edu
Telephone: +1-901-6782283
Fax: +1-901-6785281

Received: March 26, 2016

Peer-review started: March 27, 2016

First decision: May 13, 2016

Revised: May 23, 2016

Accepted: June 27, 2016

Article in press: June 29, 2016

Published online: August 18, 2016

Abstract

AIM: To test antibiotic-loaded coating for efficacy in reducing bacterial biofilm and development of osteomyelitis in an orthopaedic model of implant infection.

METHODS: Phosphatidylcholine coatings loaded with 25% vancomycin were applied to washed and sterilized titanium wires 20 mm in length. A 10 mm segment was removed from rabbit radius (total = 9; 5 coated, 4 uncoated), and the segment was injected with 1×10^6 colony forming units (CFUs) of *Staphylococcus aureus* (UAMS-1 strain). Titanium wires were inserted through

the intramedullary canal of the removed segment and into the proximal radial segment and the segment was placed back into the defect. After 7 d, limbs were removed, X-rayed, swabbed for tissue contamination. Wires were removed and processed to determine attached CFUs. Tissue was swabbed and streaked on agar plates to determine bacteriological score.

RESULTS: Antibiotic-loaded coatings resulted in significantly reduced biofilm formation (4.7 fold reduction in CFUs; $P < 0.001$) on titanium wires and reduced bacteriological score in surrounding tissue (4.0 ± 0 for uncoated, 1.25 ± 0.5 for coated; $P = 0.01$). Swelling and pus formation was evident in uncoated controls at the 7 d time point both visually and radiographically, but not in antibiotic-loaded coatings.

CONCLUSION: Active antibiotic was released from coated implants and significantly reduced signs of osteomyelitic symptoms. Implant coatings were well tolerated in bone. Further studies with additional control groups and longer time periods are warranted. Antibiotic-loaded phosphatidylcholine coatings applied at the point of care could prevent implant-associated infection in orthopaedic defects.

Key words: Biofilm; Implant; Drug delivery coating; Antibiotic; Orthopaedic infection

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We report infection preventative results of a novel antibiotic-loaded coating in a severe contaminated model of orthopaedic infection. Phosphatidylcholine coatings loaded with 25% vancomycin, which can be applied to implants immediately prior to implantation, significantly reduced staphylococcal adherence to intramedullary titanium wires in rabbits. Reduction in bacterial load on implants and in tissue for antibiotic-loaded coatings accompanied reduction in swelling and pus formation. Mild inflammatory responses were noted with coated implants compared to uncoated infected controls. This preliminary short term study demonstrates the clinical potential of these broadly applicable coatings and the need for further characterization and development.

Jennings JA, Beenken KE, Skinner RA, Meeker DG, Smeltzer MS, Haggard WO, Troxel KS. Antibiotic-loaded phosphatidylcholine inhibits staphylococcal bone infection. *World J Orthop* 2016; 7(8): 467-474 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/467.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.467>

INTRODUCTION

Biofilm formation on implants continues to be a cause of orthopaedic infection^[1,2]. While the rate of infection in

some orthopaedic implants has been reported to range from 1%-10%, in some complex orthopaedic trauma requiring percutaneous devices the rate of infection may approach 30%^[3-5]. Protection of orthopaedic implants from contamination may be more successful through prevention of biofilm formation. Because microbial cells within a biofilm are less metabolically active and shielded to some degree by exopolymeric substance, there is a high concentration of persister cells with resistance to commonly used antibiotics within biofilm^[6-9]. Standard treatment practices of prophylactic systemic administration of antibiotics may not be sufficient to inhibit or treat biofilm-based infections partly due to poor vascularity in injured tissue and partly due to the increased concentrations of antimicrobials required for elimination of biofilm^[7,10,11].

Local delivery devices have been developed to achieve high concentrations of antibiotic within the potentially contaminated tissue to target biofilm^[12-14]. However, some have limitations in degradability, implant coverage, and antibiotic loading, including non-degradable polymethylmethacrylate bone cement beads^[15], degradable calcium sulfate beads^[16], sponge devices^[17], and injectable hydrogels^[18]. Local delivery coatings directly on the implant can protect the biomaterial from biofilm formation^[19-21], but may require extensive prefabrication steps.

We previously described the biofilm inhibitory nature of phosphatidylcholine coatings loaded with antibiotics, both *in vitro* and *in vivo*^[22]. When loaded with antibiotics, this coating applied at the point-of-care just prior to implantation was shown to reduce biofilm formation of *Staphylococcus aureus* (*S. aureus*) and *Pseudomonas aeruginosa*, as well as prevent biofilm formation in a polymicrobial model of contamination with both microorganisms. While proof of principle was established in a soft-tissue dorsal model of implant infection, for this study our primary question was whether antibiotic-loaded coatings could successfully prevent infection in a contaminated orthopaedic model.

MATERIALS AND METHODS

Study design

Coatings were fabricated by mixing 6 g of purified phosphatidylcholine (Phospholipon 90G, Lipoid GMB, Germany) with 2 g of vancomycin through a previously described process of warming and kneading powdered antibiotics until the mixture was uniform^[22]. The mixture was loaded into open-ended syringes and sterilized by low dose (25 kGy) gamma irradiation.

Titanium wire 0.81 mm in diameter (McMaster Carr) was trimmed to 15 cm in length. Titanium wire was cleaned by washing with dish detergent, after which it was soaked in 20% nitric acid for 1 h. Wire was rinsed thoroughly in ultrapure water, sonicated in soapy water, and rinsed again three times in ultrapure water. Implants were separately packaged and autoclaved at

121 °C for 20 min for sterilization.

Animal model

Animal care and use statement: Study protocols were approved by the University of Arkansas for Medical Sciences Institutional Animal Care and Use Committee and all appropriate measures were taken to minimize pain and discomfort.

Nine New Zealand white rabbits were anesthetized with 1-2 cc of a xylazine/ketamine mixture intramuscularly for a dose range of 3-7 mg/kg xylazine and 30-40 mg/kg ketamine. Rabbits were maintained on 0.5%-3% isoflurane administered by nose cone to produce surgical anesthesia and monitored by a veterinary technician. The right forelimb of each rabbit was shaved and prepped using a betadine scrub and rinsed with 70% ethanol. An incision was made on the anterior surface of the right forelimb through the epidermis, musculature, and fascia until the radius was exposed. A 1 cm mid-radial segment was excised from the right forelimb using a miniature saw blade (Exakt, Oklahoma City, OK). The excised segment was then infected by inoculation of *S. aureus* [10 µL of 10⁷ colony forming units (CFUs)/mL; UAMS-1 strain] directly into the intramedullary canal.

Animals were divided into two treatment groups: Wire with 25% vancomycin-loaded coating ($n = 5$) or non-coated controls ($n = 4$). During surgical procedures titanium wires in the coated group were coated by direct manual application of coating through the syringe applicator. Coated or control wires were inserted into the medullary canal of the infected segment immediately after inoculation. Approximately 5 mm of wire extended through the proximal end of the segment and was inserted into the medullary canal of the intact proximal bone. The segment was then replaced in the same orientation and the wound was closed with sutures.

Rabbits were euthanized after 7 d. Forelimbs were removed and imaged by X-ray, noting signs of inflammation and swelling. A swab of the soft tissue and bone exposed was taken to determine bacteriological score of surrounding tissue. The segment was removed for retrieval of the wire and placed in 10% neutral buffered formalin for further processing. The wire was rinsed in sterile phosphate buffered saline (PBS) and sonicated in 5 mL of PBS for enumeration of viable CFUs attached as biofilm. The remaining forelimb was also trimmed and fixed in formalin for histological characterization. Fixed tissue was decalcified in ethylenediaminetetraacetic acid and stained with hematoxylin and eosin as well as a modified Gram stain^[23]. Images taken at 4 × magnification were scored by three independent blinded reviewers for severity of inflammatory response on a scale of 0-4.

Statistical analysis

Mann-Whitney nonparametric *t* tests in Sigma Plot were used to determine whether there were statistically

significant differences in colony counts in coated wires compared to uncoated control wires. Mann-Whitney tests were also used to determine statistical differences in bacteriological score and histological scores. Using results of previous studies determining log fold reduction of CFUs in response to antimicrobials^[24], an a priori power analysis was performed using Sigma Plot. Assuming a standard deviation of 1 unit in log-transformed CFU counts, 4 animals per group are required to have 80% power to detect a difference of 2.5 units between the control and each of the 4 experimental treatment groups at a significance level of 5%. The statistical methods of this study were reviewed by Jessica Amber Jennings of the University of Memphis.

RESULTS

After the 7 d implantation period, animals with uncoated implants were noted to have characteristics indicative of inflammation such as swelling (Figure 1), redness, and increased temperature, compared to those with implants coated with vancomycin-loaded phosphatidylcholine. Pus formation was evident in muscle tissue of several animals with uncoated wires.

Bacteriological scores confirmed that there were statistically significant reductions in bacteria recovered from surrounding tissue ($P = 0.01$) (Figure 2). CFU counts of *S. aureus* remaining as biofilm on Ti implants revealed that there were statistically fewer colonies retrieved from coated implants, 20 ± 21 CFUs vs 6.0×10^5 CFUs in the control group ($P < 0.001$) (Figure 3). Complete clearance of attached *S. aureus* biofilm was achieved in 40% of the coated wires vs 0% in the control group.

In histological specimens, evidence of inflammatory cell infiltration was evident in many of the control groups with confirmed bacterial presence, while inflammatory cell presence was minimal in the groups with vancomycin coating ($P < 0.001$) (Figure 4). Representative histological slides show severe infiltration of inflammatory cells in uncoated groups and evidence of Gram-positive staphylococci in the tissue surrounding the implant and in the cortical bone (Figure 5). Although some evidence of Gram-positive staphylococci was observed in the cortical bone of animals with antibiotic coated implants, the tissue surrounding the implant had minimal evidence of bacteria.

DISCUSSION

Successful function of orthopaedic implants can be threatened by infections, which are not always prevented by systemic antibiotic treatment^[25-27]. Implant coatings are among the local drug delivery strategies that aim to prevent or treat colonization of implants with biofilm bacteria^[21,28,29]. The naturally-derived material phosphatidylcholine has not been approved by the Food and Drug Administration (FDA) as a carrier of antibiotics,

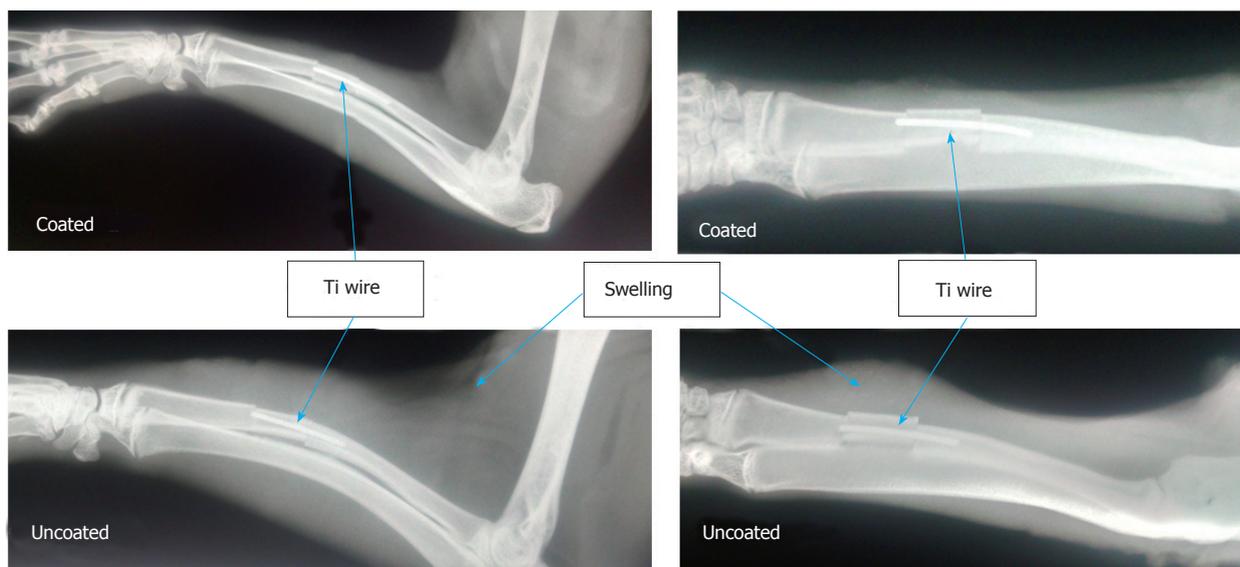


Figure 1 Representative radiographs from implant-associated osteomyelitis model after 7 d in antibiotic-coated group (top) and uncoated control group (bottom). Location of Ti wires and swelling in tissue surrounding implants are noted by arrows.

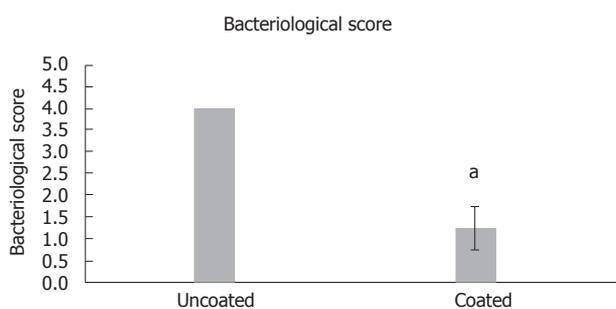


Figure 2 Graphical representation of bacteriological scores from surrounding tissue on a 0-4 point scale. Data is represented as mean \pm SD. Statistically significant difference between groups was determined by Mann-Whitney Rank Sum test ($^*P < 0.05$).

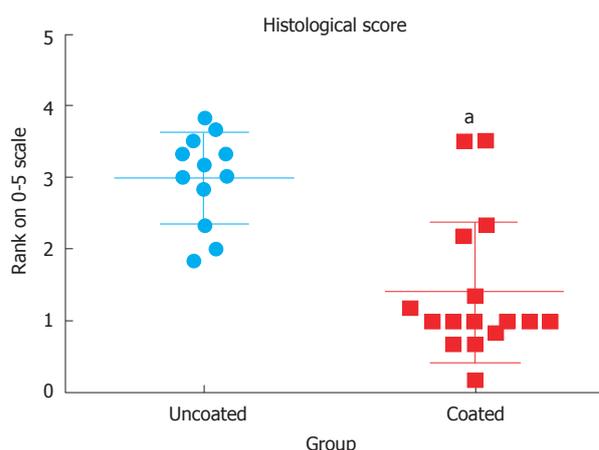


Figure 4 Plot of histological scores for uncoated and coated groups. Statistically significant difference between groups was determined by Mann-Whitney Rank Sum test ($^*P < 0.05$).

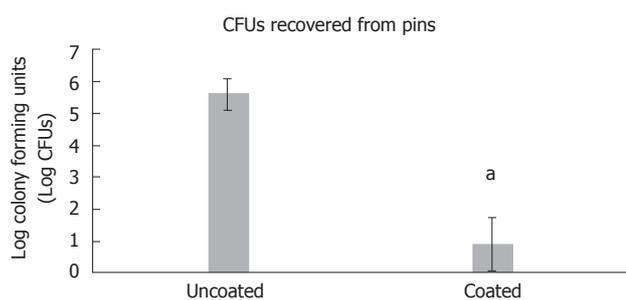


Figure 3 Graphical representation of log colony forming units retrieved from Ti wires. Data is represented as mean \pm SD. Statistically significant difference between groups was determined by Mann-Whitney Rank Sum test ($^*P < 0.05$). CFUs: Colony forming units.

but is a component of FDA approved matrices for demineralized bone graft materials^[30]. Confirming results of previous preliminary studies^[22], this initial study of a novel antibiotic loaded coating further recommends the potential of the coating to prevent implant-associated osteomyelitis.

This study demonstrates significant reduction in contamination and progression of disease, though some bacteria were recovered from the cortical bone and observed in the Gram stains. Any remaining bacteria could potentially rebound and lead to osteomyelitis. We chose vancomycin as the first antibiotic to evaluate in this coated implant model due to the known susceptibility of this strain of bacteria^[24]. We have demonstrated previously that the coating can be loaded with different antibiotics or combinations of antibiotics such as amikacin, although the release profile may vary based on solubility or other chemical properties of the antimicrobial^[22]. In the context of preventing biofilm, vancomycin has lower efficacy than antibiotics such as daptomycin^[24] though it is commonly used as an adjunctive therapy in local drug delivery devices or even sprinkled into a surgical site after implantation of

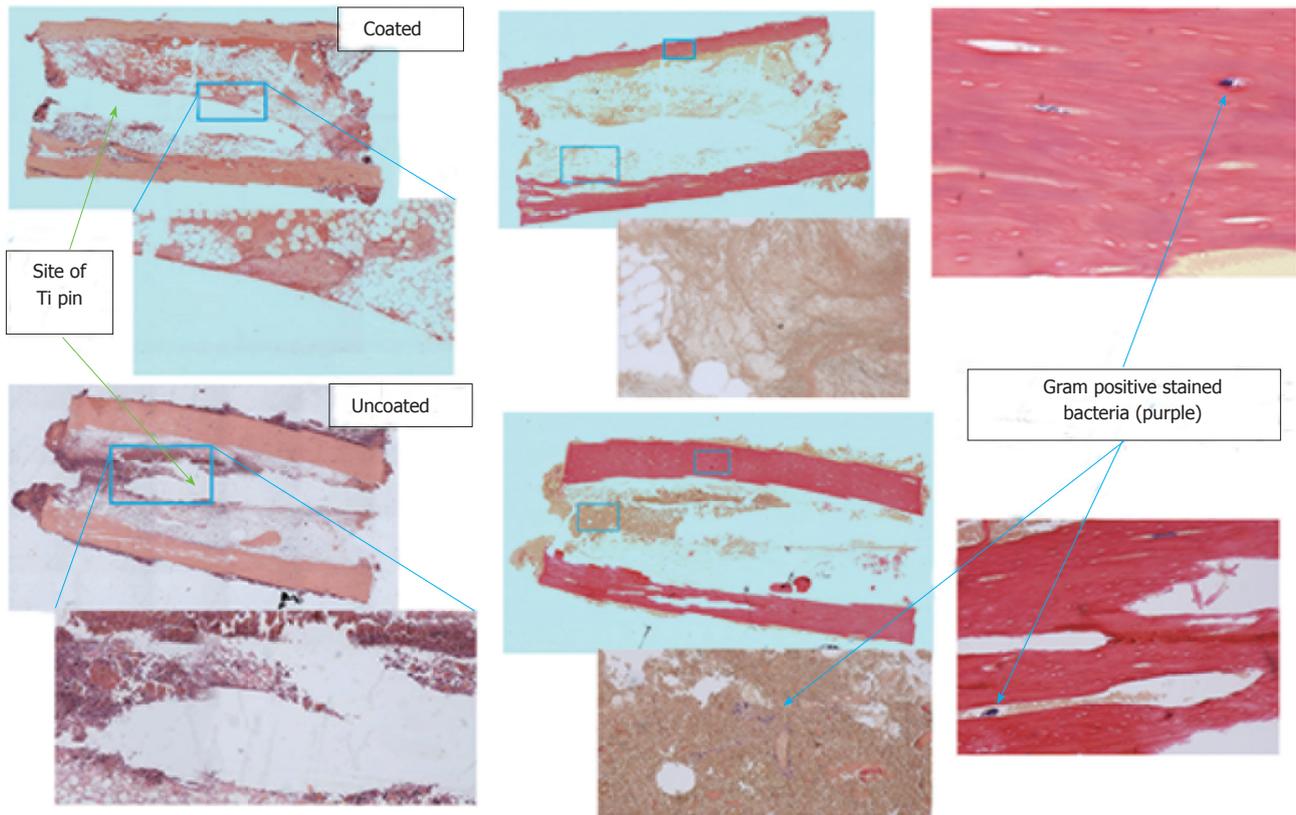


Figure 5 Photomicrographs of sections of decalcified bone stained with hematoxylin and eosin and the modified Gram stain at 4 × and 10 ×. Approximate areas of higher magnification are denoted by blue boxes. Areas where pin was removed and areas of visible staphylococci are marked with arrows.

orthopaedic devices^[31-34]. An advantage of this coating is that it may provide clinicians with a choice of antibiotic- or antimicrobial-loaded coating based on patient assessment and risk evaluation. Recently, investigations into biofilm inhibitors such as cis 2-decenoic acid, D-amino acids, and farnesol have offered potential therapeutic options to specifically target biofilm^[35-37]. The phosphatidylcholine coating could serve as delivery system for combined therapy with antibiotics and biofilm inhibitors, since additive and synergistic prevention of biofilm and bacterial growth have been demonstrated *in vitro*^[38-42].

The results of this study confirm that the results of our previous *in vitro* and soft-tissue *in vivo* studies of this coating are applicable within an orthopaedic implant context. Inflammatory response was typical of normal infiltration of inflammatory cells during the healing process^[43] and was reduced compared to when active infection was present. During implantation procedures used in this study, the manual application of coating was sufficient to retain antibiotic for local release. *In vitro* simulations of implant scenarios or alternative orthopaedic models^[44-46] may be useful in determining coating retention during intra-cortical implantation procedures such as fixation nails or bone screws. The lipid-based coating can be applied to different surfaces, though differences in adhesion to the surface and elution from different surfaces have not been fully

characterized. Future studies will evaluate the properties of the coatings on different surfaces other than metal commonly used in orthopaedic applications, such as polyether ether ketone polymer or hydroxyapatite ceramic biomaterials.

Our results should be interpreted in light of the limitations of this preliminary study. A short duration with a small number of samples in each group was selected for this initial evaluation of only 7 d. For this pilot study, we powered the study to detect large differences in remaining bacteria, but this study should be repeated for robust results. While this model has been used previously and confirmed to lead to osteomyelitic infection without an implant^[47,48], previous studies have monitored disease progression and treatment of existing infection after 3 or more weeks post-inoculation. Since the ulnar bone is still intact, the implant does not provide stability to the defect but provides a surface on which biofilm can form, so that animals return to normal activity hours after recovery without the need for fixation devices. Since the focus of this study was prevention of osteomyelitis in an implant-associated infection model, we selected an early time point at which histological and microbiological differences could still be observed^[49]. Further studies expanding on these preliminary results should include increased animal numbers and longer durations of implantation, as well as non-contaminated control groups for comparison.

The development of this model has been refined so the strain of *S. aureus* and the amount of CFUs in the inoculum results in significant evidence of infection in more than 75% of rabbits^[49]. Although this provides consistent results for evaluation of anti-infection therapy, it may not be representative of the clinical scenario where infection occurs at much lower rates and presumably with fewer contaminating bacteria. The evidence in this study demonstrating that the antibiotic coating does prevent bacterial growth even in this model of high levels of contamination indicates the clinical potential of this coating. Further, while we did observe histology for uncoated and coated groups to note any potential inflammatory responses, there were no non-antibiotic loaded coatings used as controls or defects without contamination to monitor inflammatory response in this preliminary study. Since this material has been used as a component of bone graft substitutes without issues of severe inflammation^[30], it is expected that a degradable thin coating on the implant surface would not lead to negative tissue response and may even stimulate bone growth and healing around the implant. Further studies expanding on these preliminary results should include longer durations of implantation as well as non-contaminated control groups for comparison.

In conclusion, vancomycin-loaded phosphatidylcholine coatings effectively reduced bacterial biofilm formation in an orthopaedic implant-associated model of infection. Local release of antibiotic inhibits bacterial growth and inhibits biofilm formation on the implant. These easily-applied coatings can be used at the time of surgery to prevent orthopaedic infection and improve patient outcomes.

ACKNOWLEDGMENTS

The authors wish to thank Michael Harris, Elysia Masters, Allen Mamaril, and Jonathan Tapp for assistance with histological imaging and scoring.

COMMENTS

Background

Infections associated with medical implants can pose severe threats to patient health. Methods to prevent attachment of bacteria and the formation of biofilm on implants could prevent life-threatening musculoskeletal infections. Phosphatidylcholine coatings can be loaded with antibiotics to protect the implant and surrounding tissue from pathogenic microorganisms.

Research frontiers

Phosphatidylcholine is a naturally-derived lipophilic material that forms a thin layer when manually applied to an implant surface. The point-of-care application provides versatility for use on various implant types and with many different types of antimicrobial molecules.

Innovations and breakthroughs

Compared to systemic administration of antibiotics, local delivery provides high concentrations of therapeutic molecules at the site of injury and potential contamination. Phosphatidylcholine provides a short-term degradable drug carrier matrix that can be directly coated on implants. Complete degradability,

as well as implant coverage and biocompatibility, are advantages over other common local drug delivery devices such as polymethylmethacrylate beads or calcium sulfate.

Applications

Results suggest that vancomycin-loaded coatings significantly inhibited staphylococcal growth in a model of implant-associated osteomyelitis, providing prophylactic drug release to prevent infection.

Terminology

Phosphatidylcholine is an amphiphilic molecule consisting of a polar head group and fatty acid tails that when purified can be fabricated into a coating material that leaves a waxy residue on the surface of a biomaterial. Biofilm forms when bacteria or other microorganisms attach to a surface, such as a metal implant or damaged tissue, and causes infection that is highly resistant to antibiotics or immune system clearance. *Staphylococcus aureus* is among the common pathogens that cause infections in the musculoskeletal system and can lead to osteomyelitis, which is infection of bone.

Peer-review

Interesting paper. This is a basic science study with a useful clinical application.

REFERENCES

- 1 **Stewart PS**, Costerton JW. Antibiotic resistance of bacteria in biofilms. *Lancet* 2001; **358**: 135-138 [PMID: 11463434]
- 2 **Brady RA**, Leid JG, Calhoun JH, Costerton JW, Shirliff ME. Osteomyelitis and the role of biofilms in chronic infection. *FEMS Immunol Med Microbiol* 2008; **52**: 13-22 [PMID: 18081847 DOI: 10.1111/j.1574-695X.2007.00357.x]
- 3 **Trampuz A**, Widmer AF. Infections associated with orthopedic implants. *Curr Opin Infect Dis* 2006; **19**: 349-356 [PMID: 16804382 DOI: 10.1097/01.qco.0000235161.85925.e8]
- 4 **Zimmerli W**. Clinical presentation and treatment of orthopaedic implant-associated infection. *J Intern Med* 2014; **276**: 111-119 [PMID: 24605880 DOI: 10.1111/joim.12233]
- 5 **Shirwaiker RA**, Springer BD, Spangehl MJ, Garrigues GE, Lowenberg DW, Garras DN, Yoo JU, Pottinger PS. A clinical perspective on musculoskeletal infection treatment strategies and challenges. *J Am Acad Orthop Surg* 2015; **23** Suppl: S44-S54 [PMID: 25808969 DOI: 10.5435/JAAOS-D-14-00379]
- 6 **Percival SL**, Hill KE, Malic S, Thomas DW, Williams DW. Antimicrobial tolerance and the significance of persister cells in recalcitrant chronic wound biofilms. *Wound Repair Regen* 2011; **19**: 1-9 [PMID: 21235682 DOI: 10.1111/j.1524-475X.2010.00651.x]
- 7 **Olson ME**, Ceri H, Morck DW, Buret AG, Read RR. Biofilm bacteria: formation and comparative susceptibility to antibiotics. *Can J Vet Res* 2002; **66**: 86-92 [PMID: 11989739]
- 8 **Costerton JW**. Introduction to biofilm. *Int J Antimicrob Agents* 1999; **11**: 217-221; discussion 237-239 [PMID: 10394973 DOI: 10.1016/S0924-8579(99)00018-7]
- 9 **Ranall MV**, Butler MS, Blaskovich MA, Cooper MA. Resolving biofilm infections: current therapy and drug discovery strategies. *Curr Drug Targets* 2012; **13**: 1375-1385 [PMID: 22664091 DOI: 10.2174/138945012803530251]
- 10 **Tabbaa SM**, Horton CO, Jeray KJ, Burg KJ. Role of vascularity for successful bone formation and repair. *Crit Rev Biomed Eng* 2014; **42**: 319-348 [PMID: 25597242 DOI: 10.1615/CritRevBiomedEng.2014011662]
- 11 **Donlan RM**. Role of biofilms in antimicrobial resistance. *ASAIO J* 2000; **46**: S47-S52 [PMID: 11110294 DOI: 10.1097/00002480-200011000-00037]
- 12 **McConoughey SJ**, Howlin RP, Wiseman J, Stoodley P, Calhoun JH. Comparing PMMA and calcium sulfate as carriers for the local delivery of antibiotics to infected surgical sites. *J Biomed Mater Res B Appl Biomater* 2015; **103**: 870-877 [PMID: 25142105 DOI: 10.1002/jbm.b.33247]
- 13 **Gogia JS**, Meehan JP, Di Cesare PE, Jamali AA. Local antibiotic

- therapy in osteomyelitis. *Semin Plast Surg* 2009; **23**: 100-107 [PMID: 20567732 DOI: 10.1055/s-0029-1214162]
- 14 **Hanssen AD**. Local antibiotic delivery vehicles in the treatment of musculoskeletal infection. *Clin Orthop Relat Res* 2005; **(437)**: 91-96 [PMID: 16056032]
 - 15 **McLaren AC**, McLaren SG, Hickmon MK. Sucrose, xylitol, and erythritol increase PMMA permeability for depot antibiotics. *Clin Orthop Relat Res* 2007; **461**: 60-63 [PMID: 17549030 DOI: 10.1097/BLO.0b013e3181123e90]
 - 16 **Orellana BR**, Hilt JZ, Puleo DA. Drug release from calcium sulfate-based composites. *J Biomed Mater Res B Appl Biomater* 2015; **103**: 135-142 [PMID: 24788686 DOI: 10.1002/jbm.b.33181]
 - 17 **Smith JK**, Moshref AR, Jennings JA, Courtney HS, Haggard WO. Chitosan sponges for local synergistic infection therapy: a pilot study. *Clin Orthop Relat Res* 2013; **471**: 3158-3164 [PMID: 23604649 DOI: 10.1007/s11999-013-2988-5]
 - 18 **Overstreet D**, McLaren A, Calara F, Vernon B, McLemore R. Local gentamicin delivery from resorbable viscous hydrogels is therapeutically effective. *Clin Orthop Relat Res* 2015; **473**: 337-347 [PMID: 25227556 DOI: 10.1007/s11999-014-3935-9]
 - 19 **Greene AH**, Bumgardner JD, Yang Y, Moseley J, Haggard WO. Chitosan-coated stainless steel screws for fixation in contaminated fractures. *Clin Orthop Relat Res* 2008; **466**: 1699-1704 [PMID: 18443893 DOI: 10.1007/s11999-008-0269-5]
 - 20 **Ketonis C**, Parvizi J, Jones LC. Evolving strategies to prevent implant-associated infections. *J Am Acad Orthop Surg* 2012; **20**: 478-480 [PMID: 22751167 DOI: 10.5435/JAAOS-20-07-478]
 - 21 **Norowski PA**, Courtney HS, Babu J, Haggard WO, Bumgardner JD. Chitosan coatings deliver antimicrobials from titanium implants: a preliminary study. *Implant Dent* 2011; **20**: 56-67 [PMID: 21278528]
 - 22 **Jennings JA**, Carpenter DP, Troxel KS, Beenken KE, Smeltzer MS, Courtney HS, Haggard WO. Novel Antibiotic-loaded Point-of-care Implant Coating Inhibits Biofilm. *Clin Orthop Relat Res* 2015; **473**: 2270-2282 [PMID: 25604874 DOI: 10.1007/s11999-014-4130-8]
 - 23 **Skinner RA**, Hickmon SG, Nelson CL, Germer RA. Modified stain for identification of staphylococcus-aureus in osteomyelitis. *J Histotechnol* 1992; **15**: 303-306
 - 24 **Weiss EC**, Spencer HJ, Daily SJ, Weiss BD, Smeltzer MS. Impact of sarA on antibiotic susceptibility of Staphylococcus aureus in a catheter-associated in vitro model of biofilm formation. *Antimicrob Agents Chemother* 2009; **53**: 2475-2482 [PMID: 19289527]
 - 25 **Sabath LD**, Garner C, Wilcox C, Finland M. Susceptibility of Staphylococcus aureus and Staphylococcus epidermidis to 65 antibiotics. *Antimicrob Agents Chemother* 1976; **9**: 962-969 [PMID: 938025]
 - 26 **Campoccia D**, Montanaro L, Arciola CR. The significance of infection related to orthopedic devices and issues of antibiotic resistance. *Biomaterials* 2006; **27**: 2331-2339 [PMID: 16364434 DOI: 10.1016/j.biomaterials.2005.11.044]
 - 27 **McConoughey SJ**, Howlin R, Granger JF, Manring MM, Calhoun JH, Shirliff M, Kathju S, Stoodley P. Biofilms in periprosthetic orthopedic infections. *Future Microbiol* 2014; **9**: 987-1007 [PMID: 25302955 DOI: 10.2217/fmb.14.64]
 - 28 **Ketonis C**, Barr S, Adams CS, Shapiro IM, Parvizi J, Hickok NJ. Vancomycin bonded to bone grafts prevents bacterial colonization. *Antimicrob Agents Chemother* 2011; **55**: 487-494 [PMID: 21098245 DOI: 10.1128/AAC.00741-10]
 - 29 **Adams CS**, Antoci V, Harrison G, Patal P, Freeman TA, Shapiro IM, Parvizi J, Hickok NJ, Radin S, Ducheyne P. Controlled release of vancomycin from thin sol-gel films on implant surfaces successfully controls osteomyelitis. *J Orthop Res* 2009; **27**: 701-709 [PMID: 19051247 DOI: 10.1002/jor.20815]
 - 30 **Han B**, Tang B, Nimni ME. Combined effects of phosphatidylcholine and demineralized bone matrix on bone induction. *Connect Tissue Res* 2003; **44**: 160-166 [PMID: 14504036]
 - 31 **Molinari RW**, Khera OA, Molinari WJ. Prophylactic intraoperative powdered vancomycin and postoperative deep spinal wound infection: 1,512 consecutive surgical cases over a 6-year period. *Eur Spine J* 2012; **21** Suppl 4: S476-S482 [PMID: 22160172 DOI: 10.1007/s00586-011-2104-z]
 - 32 **Giavaresi G**, Bertazzoni Minelli E, Sartori M, Benini A, Della Bora T, Sambri V, Gaibani P, Borsari V, Salamanna F, Martini L, Nicoli Aldini N, Fini M. Microbiological and pharmacological tests on new antibiotic-loaded PMMA-based composites for the treatment of osteomyelitis. *J Orthop Res* 2012; **30**: 348-355 [PMID: 21882237 DOI: 10.1002/jor.21531]
 - 33 **Penn-Barwell JG**, Murray CK, Wenke JC. Local antibiotic delivery by a bioabsorbable gel is superior to PMMA bead depot in reducing infection in an open fracture model. *J Orthop Trauma* 2014; **28**: 370-375 [PMID: 23948961 DOI: 10.1097/BOT.0b013e3182a7739e]
 - 34 **Gitelis S**, Brebach GT. The treatment of chronic osteomyelitis with a biodegradable antibiotic-impregnated implant. *J Orthop Surg (Hong Kong)* 2002; **10**: 53-60 [PMID: 12401922]
 - 35 **Davies DG**, Marques CN. A fatty acid messenger is responsible for inducing dispersion in microbial biofilms. *J Bacteriol* 2009; **191**: 1393-1403 [PMID: 19074399 DOI: 10.1128/JB.01214-08]
 - 36 **Hochbaum AI**, Kolodkin-Gal I, Foulston L, Kolter R, Aizenberg J, Losick R. Inhibitory effects of D-amino acids on Staphylococcus aureus biofilm development. *J Bacteriol* 2011; **193**: 5616-5622 [PMID: 21856845 DOI: 10.1128/jb.05534-11]
 - 37 **Koo H**, Hayacibara MF, Schobel BD, Cury JA, Rosalen PL, Park YK, Vacca-Smith AM, Bowen WH. Inhibition of Streptococcus mutans biofilm accumulation and polysaccharide production by apigenin and tt-farnesol. *J Antimicrob Chemother* 2003; **52**: 782-789 [PMID: 14563892 DOI: 10.1093/jac/dkg449]
 - 38 **Jennings JA**, Courtney HS, Haggard WO. Cis-2-decenoic acid inhibits S. aureus growth and biofilm in vitro: a pilot study. *Clin Orthop Relat Res* 2012; **470**: 2663-2670 [PMID: 22585351 DOI: 10.1007/s11999-012-2388-2]
 - 39 **Rahmani-Badi A**, Sepehr S, Mohammadi P, Soudi MR, Babaie-Naiej H, Fallahi H. A combination of cis-2-decenoic acid and antibiotics eradicates pre-established catheter-associated biofilms. *J Med Microbiol* 2014; **63**: 1509-1516 [PMID: 25082943 DOI: 10.1099/jmm.0.075374-0]
 - 40 **Sanchez CJ**, Akers KS, Romano DR, Woodbury RL, Hardy SK, Murray CK, Wenke JC. D-amino acids enhance the activity of antimicrobials against biofilms of clinical wound isolates of Staphylococcus aureus and Pseudomonas aeruginosa. *Antimicrob Agents Chemother* 2014; **58**: 4353-4361 [PMID: 24841260 DOI: 10.1128/AAC.02468-14]
 - 41 **Jabra-Rizk MA**, Meiller TF, James CE, Shirliff ME. Effect of farnesol on Staphylococcus aureus biofilm formation and antimicrobial susceptibility. *Antimicrob Agents Chemother* 2006; **50**: 1463-1469 [PMID: 16569866 DOI: 10.1128/AAC.50.4.1463-1469.2006]
 - 42 **Estrela AB**, Abraham WR. Combining biofilm-controlling compounds and antibiotics as a promising new way to control biofilm infections. *Pharmaceuticals* 2010; **3**: 1374-1393 [DOI: 10.3390/ph3051374]
 - 43 **Anderson JM**, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. *Semin Immunol* 2008; **20**: 86-100 [PMID: 18162407 DOI: 10.1016/j.smim.2007.11.004]
 - 44 **Berenthal NM**, Stavrakis AI, Billi F, Cho JS, Kremen TJ, Simon SI, Cheung AL, Finerman GA, Lieberman JR, Adams JS, Miller LS. A mouse model of post-arthroplasty Staphylococcus aureus joint infection to evaluate in vivo the efficacy of antimicrobial implant coatings. *PLoS One* 2010; **5**: e12580 [PMID: 20830204 DOI: 10.1371/journal.pone.0012580]
 - 45 **Prabhakara R**, Harro JM, Leid JG, Harris M, Shirliff ME. Murine immune response to a chronic Staphylococcus aureus biofilm infection. *Infect Immun* 2011; **79**: 1789-1796 [PMID: 21282411 DOI: 10.1128/IAI.01386-10]
 - 46 **Lazzarini L**, Overgaard KA, Conti E, Shirliff ME. Experimental osteomyelitis: what have we learned from animal studies about the systemic treatment of osteomyelitis? *J Chemother* 2006; **18**: 451-460 [PMID: 17127219 DOI: 10.1179/joc.2006.18.5.451]
 - 47 **Blevins JS**, Elasri MO, Allmendinger SD, Beenken KE, Skinner RA, Thomas JR, Smeltzer MS. Role of sarA in the pathogenesis of Staphylococcus aureus musculoskeletal infection. *Infect Immun* 2003; **71**: 516-523 [PMID: 12496203]
 - 48 **Beenken KE**, Smith JK, Skinner RA, McLaren SG, Bellamy W, Gruenwald MJ, Spencer HJ, Jennings JA, Haggard WO,

Jennings JA *et al.* Implant coating prevents infection

Smeltzer MS. Chitosan coating to enhance the therapeutic efficacy of calcium sulfate-based antibiotic therapy in the treatment of chronic osteomyelitis. *J Biomater Appl* 2014; **29**: 514-523 [PMID: 24854984 DOI: 10.1177/0885328214535452]

49 **Smeltzer MS**, Thomas JR, Hickmon SG, Skinner RA, Nelson CL, Griffith D, Parr TR, Evans RP. Characterization of a rabbit model of staphylococcal osteomyelitis. *J Orthop Res* 1997; **15**: 414-421 [PMID: 9246088 DOI: 10.1002/jor.1100150314]

P- Reviewer: Elgafy H, Papachristou GC, Vulcano E
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Wu HL



Basic Study

Using simulation to train orthopaedic trainees in non-technical skills: A pilot study

Samuel R Heaton, Zoe Little, Kash Akhtar, Manoj Ramachandran, Joshua Lee

Samuel R Heaton, Zoe Little, Kash Akhtar, Manoj Ramachandran, Joshua Lee, Centre for Orthopaedics, Royal London Hospital, Barts Health NHS Trust, London E1 1BB, United Kingdom

Author contributions: Heaton SR and Akhtar K drafted the manuscript; Little Z collated the statistics; Ramachandran M and Lee J designed the course.

Institutional review board statement: All participant questionnaires were obtained with the informed consent from the candidates with express permission for this paper. All responses are anonymised. There was no requirement for ethical approval as this was purely a questionnaire of doctors experiences of a course.

Informed consent statement: All involved persons gave their verbal informed consent prior to study inclusion. All study responses were anonymised.

Conflict-of-interest statement: To the best of our knowledge, no conflict of interest exists.

Data sharing statement: Dataset and course specifics are available from the corresponding author. Participant consent was obtained to share the data but all feedback data is anonymous.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Samuel R Heaton, FRCS, Centre for Orthopaedics, Royal London Hospital, Barts Health NHS Trust, Whitechapel Road, London E1 1BB, United Kingdom. samheaton@hotmail.com
Telephone: +44-20-73777000

Received: February 15, 2016

Peer-review started: February 16, 2016

First decision: March 24, 2016

Revised: April 5, 2016

Accepted: June 1, 2016

Article in press: June 3, 2016

Published online: August 18, 2016

Abstract

AIM: To enhance non-technical skills and to analyse participant's experience of a course tailored for orthopaedic surgeons.

METHODS: A Delphi technique was used to develop a course in human factors specific to orthopaedic residents. Twenty-six residents (six per course) participated in total with seven course facilitators all trained in Crisis Resource Management providing structured feedback. Six scenarios recreated challenging real-life situations using high-fidelity mannequins and simulated patients. Environments included a simulated operating suite, clinic room and ward setting. All were undertaken in a purpose built simulation suite utilising actors, mock operating rooms, mock clinical rooms and a high fidelity adult patient simulator organised through a simulation control room. Participants completed a 5-point Likert scale questionnaire (strongly disagree to strongly agree) before and after the course. This assessed their understanding of non-technical skills, scenario validity, relevance to orthopaedic training and predicted impact of the course on future practice. A course evaluation questionnaire was also completed to assess participants' feedback on the value and quality of the course itself.

RESULTS: Twenty-six orthopaedic residents participated (24 male, 2 female; post-graduation 5-10 years), mean year of residency program 2.6 out of 6 years required in the United Kingdom. Pre-course questionnaires showed

that while the majority of candidates recognised the importance of non-technical (NT) skills in orthopaedic training they demonstrated poor understanding of non-technical skills and their role. This improved significantly after the course (Likert score 3.0-4.2) and the perceived importance of these skills was reported as good or very good in 100%. The course was reported as enjoyable and provided an unthreatening learning environment with the candidates placing particular value on the learning opportunity provided by reflecting on their performance. All agreed that the course achieved its intended aims with realistic simulation scenarios. Participants believed patient care, patient safety and team working would all improve with further human factors training (4.4-4.6). and felt that NT skills learnt through simulation-based training should become an integral component of their training program.

CONCLUSION: Participants demonstrated improved understanding of non-technical performance, recognised its relevance to patient safety and expressed a desire for its integration in training.

Key words: Teaching; Learning; Simulation; Non-technical; Surgery

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We have developed what we believe to be the first non-technical skills course specifically catering to the unique issues affecting orthopaedic surgeons in everyday practice. Participants demonstrated an improved understanding of the importance of non-technical performance, recognised its relevance to improving patient safety and expressed a desire for it to become an integral part of training. Non-technical skills training may also provide a means of identifying and supporting trainees in difficulty.

Heaton SR, Little Z, Akhtar K, Ramachandran M, Lee J. Using simulation to train orthopaedic trainees in non-technical skills: A pilot study. *World J Orthop* 2016; 7(8): 475-480 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/475.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.475>

INTRODUCTION

Non-technical (NT) skills are those abilities of a surgeon that may influence performance but do not relate directly to clinical knowledge or surgical technique. These "human factors" can be divided into cognitive skills or social skills and include situational awareness, decision-making, communication, teamwork and leadership^[1].

Such interpersonal skills have traditionally been overlooked in training programs, with a premium placed on technical skills such as surgical dexterity, clinical expertise and factual knowledge. While these

are essential factors in successful and safe patient interactions, there is increasing evidence that sub-optimal human factors can have negative effects on final patient outcomes. This can lead to adverse events during surgery and also during patient or staff interactions^[2]. Communication errors have been shown to be causal factors for up to 43% of surgical errors^[3], which suggests that technical skills alone are not sufficient to minimise risk sufficiently.

NT skills have already been noted to be of importance in non-medical fields and within some medical specialities. The National Aeronautics and Space Administration found that 70% of errors in the aviation industry were due to human factors such as failures in communication, leadership and decision-making^[4]. This led to the development of Crew Resource Management (CRM) training in order to enable individuals to manage human performance limits and improve safety. CRM training has subsequently been adopted in the manufacturing, military and nuclear industries^[5], civil aviation and oil exploration^[6]. The anaesthetics community^[7,8] has largely driven CRM in medicine with the development of Anaesthetic Crisis Resource Management^[9]. This allows a participant to practice team-training skills in a simulated environment and then receive feedback on their performance. This has been well received with the significant majority of people confirming it has benefited their regular practice^[10]. Cardiac surgery^[11], operating room personnel^[12,13], general surgery^[14,15], nursing^[16], obstetrics^[17] and undergraduate medical curricula^[18] are all increasingly recognising the importance of NT skills.

The Royal College of Surgeons of Edinburgh has produced a course designed for surgeons called NOTSS: Non-Technical Skills for Surgeons. It rates behaviour in surgeons and evaluates various non-technical skills with feedback given by consultants (attendings) based on structured observations^[19]. A scoring system has been developed termed the Oxford Non-Technical Skills scale^[20], which solely focuses on team work in an operating theatre. It is therefore somewhat surprising that the only specific orthopaedic communication roles in routine training are limited to the Advanced Trauma Life Support simulated moulages, which are still heavily loaded towards technical skills.

MATERIALS AND METHODS

Participants

Twenty-six orthopaedic residents participated in total. The faculty consisted of three orthopaedic attendings, one senior resident and three full-time course facilitators from the department of medical simulation trained in Crisis Resource Management. Each course was undertaken with six participants and seven staff members.

Course structure

The faculty used a Delphi technique^[21] to devise six

Table 1 Examples of scenarios used

Setting	Scenario
Clinic	Discussing a surgical complication with an upset patient
Clinic	Breaking bad news to an anxious patient
Operating room	Managing a large team in crisis during a bone cement implantation reaction
Operating room	Dealing with an intoxicated senior colleague
Ward	Managing team members in a critically ill patient setting
Ward	Making a complex referral to an obstructive colleague

scenarios occurring in a realistic physical environment supported by a multidisciplinary team. These were based on actual events experienced by faculty members or reported in the General Medical Council archives^[22] and were designed to immerse participants in the scenario and represent real-life challenging situations so as to test trainees' NT skills across the range (Table 1).

Each participant agreed to be filmed for feedback purposes and signed a confidentiality agreement. They then filled in a pre-course questionnaire about their understanding of NT skills. An introductory presentation was delivered by the course leader describing the aims of the course and the outline for the day's activities.

The scenarios were viewed directly through one-way screens by the other candidates and faculty members and were also concomitantly filmed for feedback purposes. Each scenario was undertaken in a purpose built simulation suite, which included a high fidelity adult patient simulator, actors as simulated patients, a mock operating room (Figure 1), outpatient clinic room or in-patient ward setting. All scenarios were controlled from the simulation control centre (Figures 2 and 3).

Two examples are described in detail below with the instructions for the candidate and the Simulated Patient plus the end point aims.

Clinic scenario 1

Discussing a surgical complication with an upset patient: (1) candidates brief. The patient has had an ankle fracture and a subsequent operation leading to chronic syndesmotic injury with pain. The original operation was poorly performed, leading to the current situation. The patient now needs revision surgery and returns to clinic today to discuss this. The patient has sent a complaint letter to the hospital demanding compensation and for the initial surgeon to be disciplined. The patient is unhappy with the response they have received; (2) patients brief: You have come back for your follow-up, which is to discuss the next part of your treatment. You are not satisfied by the response you have received, you feel entitled to compensation and you want that surgeon who did the operation to be suspended; and (3) end point aim: Empathises with patient, manages the situation and the patient appropriately, explains the hospital's formal complaints procedure and how to proceed. Is aware of the formal complaints procedure. Comes to an

Table 2 Non-technical skills perceptions questionnaire

Please indicate how inclined you are to agree with the following statements
I have a good understanding of non-technical skills
Non-technical skills are important in orthopaedic training
Non-technical skills simulation should be an integral part of orthopaedic training

acceptable management plan for the clinical problem.

Operating room scenario 2

Dealing with an intoxicated senior colleague:

(1) candidates brief: You are in the operating room, the patient has received general anaesthesia and you are preparing to assist your attending in a total knee replacement. This is your first week working with this attending; (2) attending's brief: Display signs of being intoxicated and inability to keep focus on the task. If candidate does not realise the situation then scrub nurse to take them aside and express concern. If candidate asks directly if you are drunk, deny it vehemently and express annoyance at their question; (3) scrub nurse: Wait for candidate to start scrubbing and whilst consultant is fiddling with setup, suggest to the candidate that the consultant is drunk. Tell the candidate in no uncertain terms that they must take action to protect patient safety; and (4) end point aim: To prevent the attending from operating. Arrange for another surgeon or decide to abandon the procedure and wake up the patient. Put patient safety first followed by duty of care to colleague. Plan for discussion with department director and suggest occupational health referral. Keep accurate and appropriate records (Figure 3).

Questionnaires

All questions were answered on a 5 point Likert-type scale (strongly disagree to strongly agree). A questionnaire (Table 2) was designed to determine participants' understanding of NT skills and their perceptions of the relevance and importance of these in orthopaedics, both before and after training.

A course evaluation questionnaire (Table 3) was designed to assess participants' feedback on the value and quality of the course.

A debriefing session was conducted after each scenario, during which the participant reflected on their own performance and received constructive feedback from their peers and the faculty. Following debriefing after the final scenario of the day, the NT skills perception questionnaire was completed again, together with the course evaluation questionnaire.

RESULTS

Twenty-six participants took part, 24 were male and 2 were female (post-graduation 5-10). The mean year of



Figure 1 Mock operating room with viewing room behind one way mirror.



Figure 2 Simulation control centre.



Figure 3 A typical operating room scenario used during the course.

training on the residency program was 2.6 (out of the 6 training years required in the United Kingdom).

Understanding and perception of NT skills

In terms of the understanding Prior to the course, the

majority of participants recognised the importance of NT skills in orthopaedic training but only 42% reported a good understanding of them. The course increased the reported understanding of NT skills and further emphasised their importance in orthopaedic training.

Table 3 Course evaluation questionnaire	
Please indicate how inclined you are to agree with the following statements	
I enjoyed this simulation day	
It was useful to reflect on my performance	
The course met the initial aims as presented in the introductory lecture	
I thought the simulation scenarios were realistic	
Simulation provided an unthreatening learning environment	
This course will improve my team working	
This course will improve my practice in terms of patient care	
This course will improve my practice in terms of patient safety	

Table 4 Results of the course evaluation questionnaire	
Please indicate how inclined you are to agree with the following statements	Agree or strongly agree (%)
I enjoyed this simulation day	100
It was useful to reflect on my performance	100
The course met the initial aims as presented in the introductory lecture	100
I thought the simulation scenarios were realistic	92
Simulation provided an unthreatening learning environment	96
This course will improve my team working	88
This course will improve my practice in terms of patient care	88
This course will improve my practice in terms of patient safety	88

Moreover, all participants valued NT skills and thought that simulation-based training should become an integral component of orthopaedic training (Figure 4).

Course value and quality

All participants enjoyed the course and valued reflecting on their performance. All agreed or strongly agreed that the course achieved its intended aims (Table 4).

The majority found the simulation scenarios realistic and all but one reported that the course provided an unthreatening learning environment. Furthermore, 88% of participants agreed or strongly agreed that the course would improve their clinical practice in terms of team working, patient care and patient safety.

DISCUSSION

We have developed and piloted a new NT skills simulation course specifically for orthopaedic trainees. This simulation-based training was shown to provide a realistic, enjoyable and unthreatening learning environment and was well accepted by trainees. Course participants were able to reflect on their performances in various clinical scenarios and to improve their understanding of NT skills. The majority of those taking part felt that the course would improve team working and patient care. Their perception of the relevance of NT skills to orthopaedic training and their importance in clinical practice became more positive after experiencing the course. Participants demonstrated an improved

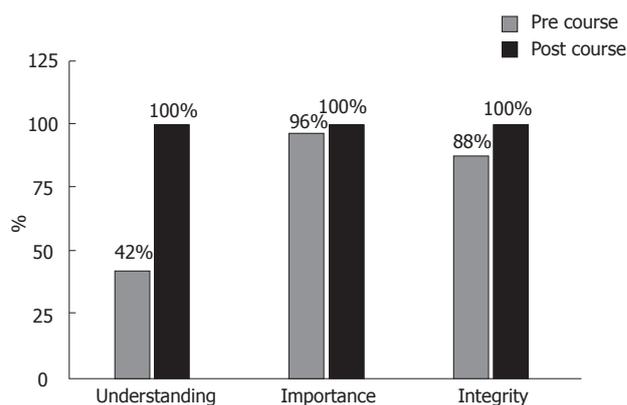


Figure 4 Results of the pre- and post- non-technical skills perceptions questionnaire shown in table 2 (percentage declaring “agree” or “strongly agree”).

understanding of the importance of non-technical performance, recognised its relevance to improving patient safety and expressed a desire for it to become a part of their training.

The purpose of this course was to provide teaching and feedback on NT skills specific to orthopaedic surgery with immersion in high fidelity environments simulating the operating room and outpatient clinic settings. The participants were shown the importance of NT skills in routine practice and were able to demonstrate and practice these skills in a safe environment, without posing risk to patients. They were able to critically evaluate their own performances and those of others, as well as receiving guided feedback from the experienced faculty. This allowed identification of areas for consolidation or improvement in order to prepare trainees for more senior clinical roles.

The importance of reflection in clinical training continues to grow and it is invaluable for surgeons of all grades to reflect on their own practice in order to ensure ongoing professional and personal development, as well as improvement in their practice.

It has been proposed that learners can be helped stepwise through this learning cycle by the creation of appropriate experiences and by assessment and feedback to facilitate transformation^[23]. A training programme such as outlined in this paper can be one way of achieving this safely.

There is relatively little emphasis on NT skills in the orthopaedic literature, although their importance in obtaining successful clinical outcomes is clear and well recognised in many high-risk fields. We have described a way to use simulation to develop NT skills in orthopaedics in a risk-free environment and this was well received by trainees. Similar NT skills courses exist in other medical specialties, but this is the first we are aware of to focus specifically on the unique issues affecting orthopaedic surgeons. This course is becoming an integral component of our registrar training programme and may also provide a means for identifying and supporting the trainee in difficulty.

There is growing evidence for NT skills to be embedded into the orthopaedic training curriculum and the use of simulation may be a means of achieving this.

ACKNOWLEDGMENTS

We thank the Barts Simulation team who facilitated the course at the Education Academy Simulation centre at the Royal London Hospital.

COMMENTS

Background

Non-technical skills include situational awareness, decision-making, communication, teamwork and leadership. Evidence suggests these attributes are the key to reducing errors and avoiding adverse events.

Research frontiers

Training in non-technical skills is widely used in many high-risk industries and some medical specialties. Simulation-based training in the orthopaedic community is based predominantly on technical skills such as dexterity with little emphasis on human factors training.

Innovations and breakthroughs

The authors have developed what they believe to be the first non-technical skills course specifically catering to the unique issues affecting orthopaedic surgeons in everyday practice.

Terminology

Non-technical skills include situational awareness, decision-making, communication, teamwork and leadership.

Peer-review

The paper is very well presented.

REFERENCES

- 1 Yule S, Flin R, Maran N, Rowley D, Youngson G, Paterson-Brown S. Surgeons' non-technical skills in the operating room: reliability testing of the NOTSS behavior rating system. *World J Surg* 2008; **32**: 548-556 [PMID: 18259809 DOI: 10.1007/s00268-007-9320-z]
- 2 Christian CK, Gustafson ML, Roth EM, Sheridan TB, Gandhi TK, Dwyer K, Zinner MJ, Dierks MM. A prospective study of patient safety in the operating room. *Surgery* 2006; **139**: 159-173 [PMID: 16455323 DOI: 10.1016/j.surg.2005.07.037]
- 3 Gawande AA, Zinner MJ, Studdert DM, Brennan TA. Analysis of errors reported by surgeons at three teaching hospitals. *Surgery* 2003; **133**: 614-621 [PMID: 12796727 DOI: 10.1067/msy.2003.169]
- 4 Helmreich RL, Merritt AC, Wilhelm JA. The evolution of Crew Resource Management training in commercial aviation. *Int J Aviat Psychol* 1999; **9**: 19-32 [PMID: 11541445]
- 5 Flin R, O'Connor P, Mearns K. Crew resource management: improving safety in high reliability industries. *Team Performance Management* 2002; **8**: 68-78 [DOI: 10.1108/13527590210433366]
- 6 Flin R, Goeters K, Amalberti R. The development of the NOTECHS system for evaluating pilots' CRM skills. *Human Factors and Aerospace Safety* 2003; **3**: 95-117
- 7 Fletcher GC, McGeorge P, Flin RH, Glavin RJ, Maran NJ. The role of non-technical skills in anaesthesia: a review of current literature. *Br J Anaesth* 2002; **88**: 418-429 [PMID: 11990277 DOI: 10.1093/bja/88.3.418]
- 8 Manser T, Harrison TK, Gaba DM, Howard SK. Coordination patterns related to high clinical performance in a simulated anesthetic crisis. *Anesth Analg* 2009; **108**: 1606-1615 [PMID: 19372344 DOI: 10.1213/ane.0b013e3181981d36]
- 9 Holzman RS, Cooper JB, Gaba DM, Philip JH, Small SD, Feinstein D. Anesthesia crisis resource management: real-life simulation training in operating room crises. *J Clin Anesth* 1995; **7**: 675-687 [PMID: 8747567 DOI: 10.1016/0952-8180(95)00146-8]
- 10 Aggarwal R, Undre S, Moorthy K, Vincent C, Darzi A. The simulated operating theatre: comprehensive training for surgical teams. *Qual Saf Health Care* 2004; **13** Suppl 1: i27-i32 [PMID: 15465952 DOI: 10.1136/qshc.2004.010009]
- 11 Wahr JA, Prager RL, Abernathy JH, Martinez EA, Salas E, Seifert PC, Groom RC, Spiess BD, Searles BE, Sundt TM, Sanchez JA, Shappell SA, Culig MH, Lazzara EH, Fitzgerald DC, Thourani VH, Eghtesady P, Ikonomidis JS, England MR, Sellke FW, Nussmeier NA. Patient safety in the cardiac operating room: human factors and teamwork: a scientific statement from the American Heart Association. *Circulation* 2013; **128**: 1139-1169 [PMID: 23918255 DOI: 10.1161/CIR.0b013e3182a38efa]
- 12 Paige JT, Kozmenko V, Yang T, Gururaja RP, Hilton CW, Cohn I, Chauvin SW. Attitudinal changes resulting from repetitive training of operating room personnel using of high-fidelity simulation at the point of care. *Am Surg* 2009; **75**: 584-590; discussion 590-591 [PMID: 19655602]
- 13 Undre S, Koutantji M, Sevdalis N, Gautama S, Selvapatt N, Williams S, Sains P, McCulloch P, Darzi A, Vincent C. Multidisciplinary crisis simulations: the way forward for training surgical teams. *World J Surg* 2007; **31**: 1843-1853 [PMID: 17610109 DOI: 10.1007/s00268-007-9128-x]
- 14 Powers KA, Rehrig ST, Irias N, Albano HA, Malinow A, Jones SB, Moorman DW, Pawlowski JB, Jones DB. Simulated laparoscopic operating room crisis: An approach to enhance the surgical team performance. *Surg Endosc* 2008; **22**: 885-900 [PMID: 18071813 DOI: 10.1007/s00464-007-9678-x]
- 15 Powers K, Rehrig ST, Schwaitzberg SD, Callery MP, Jones DB. Seasoned surgeons assessed in a laparoscopic surgical crisis. *J Gastrointest Surg* 2009; **13**: 994-1003 [PMID: 19190969 DOI: 10.1007/s11605-009-0802-1]
- 16 Mitchell L, Flin R. Non-technical skills of the operating theatre scrub nurse: literature review. *J Adv Nurs* 2008; **63**: 15-24 [PMID: 18598248 DOI: 10.1111/j.1365-2648.2008.04695.x]
- 17 Robertson B, Schumacher L, Gosman G, Kanfer R, Kelley M, DeVita M. Simulation-based crisis team training for multidisciplinary obstetric providers. *Simul Healthc* 2009; **4**: 77-83 [PMID: 19444044 DOI: 10.1097/SIH.0b013e31819171cd]
- 18 Pilpel D, Schor R, Benbassat J. Barriers to acceptance of medical error: the case for a teaching program (695). *Med Educ* 1998; **32**: 3-7 [PMID: 9624392 DOI: 10.1046/j.1365-2923.1998.00695.x]
- 19 Flin R, Yule S, McKenzie L, Paterson-Brown S, Maran N. Attitudes to teamwork and safety in the operating theatre. *Surgeon* 2006; **4**: 145-151 [PMID: 16764199 DOI: 10.1016/S1479-666X(06)80084-3]
- 20 Mishra A, Catchpole K, McCulloch P. The Oxford NOTECHS System: reliability and validity of a tool for measuring teamwork behaviour in the operating theatre. *Qual Saf Health Care* 2009; **18**: 104-108 [PMID: 19342523]
- 21 de Villiers MR, de Villiers PJ, Kent AP. The Delphi technique in health sciences education research. *Med Teach* 2005; **27**: 639-643 [PMID: 16332558 DOI: 10.1080/13611260500069947]
- 22 General Medical Council archives. [accessed 2014 Dec 8]. Available from: URL: <http://www.gmc-uk.org/index.asp> accessed 12/8/14
- 23 Maudsley G, Strivens J. Promoting professional knowledge, experiential learning and critical thinking for medical students. *Med Educ* 2000; **34**: 535-544 [PMID: 10886636 DOI: 10.1046/j.1365-2923.2000.00632.x]

P- Reviewer: Drosos GI S- Editor: Qiu S L- Editor: A
E- Editor: Wu HL



Retrospective Cohort Study

Criteria for level 1 and level 2 trauma codes: Are pelvic ring injuries undertriaged?

Brittany E Haws, Scott Wuertzer, Laura Raffield, Leon Lenchik, Anna N Miller

Brittany E Haws, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, United States

Scott Wuertzer, Leon Lenchik, Department of Radiology, Medical Center Boulevard, Winston-Salem, NC 27157, United States

Laura Raffield, Department of Molecular Genetics and Genomics, Medical Center Boulevard, Winston-Salem, NC 27157, United States

Anna N Miller, Department of Orthopaedic Surgery, Medical Center Boulevard, Winston-Salem, NC 27157, United States

Author contributions: Wuertzer S, Lenchik L and Miller AN designed and performed the research; Haws BE, Raffield L and Miller AN analyzed the data; Haws BE wrote the paper with editing by the remaining authors.

Institutional review board statement: This study has been approved by the Wake Forest Medical Center Institutional Review Board.

Informed consent statement: Consent was not obtained because the presented data was anonymized and risk of identification is low.

Conflict-of-interest statement: The authors of this study do not endorse any conflicts of interest.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at behaws1@gmail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Brittany E Haws, BS, Medical Student, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, United States. behaws1@gmail.com
Telephone: +1-336-7163950
Fax: +1-336-7167310

Received: February 17, 2016
Peer-review started: February 19, 2016
First decision: March 25, 2016
Revised: April 8, 2016
Accepted: June 1, 2016
Article in press: June 3, 2016
Published online: August 18, 2016

Abstract

AIM: To determine the association of unstable pelvic ring injuries with trauma code status.

METHODS: A retrospective review of all pelvic ring injuries at a single academic center from July 2010 to June 2013 was performed. The trauma registry was used to identify level 1 and level 2 trauma codes for each injury. The computed tomography scans in all patients were classified as stable or unstable using the Abbreviated Injury Scale. Pelvic injury classifications in level 1 and level 2 groups were compared. Patient disposition at discharge in level 1 and level 2 groups were also compared.

RESULTS: There were 108 level 1 and 130 level 2 blunt trauma admissions. In the level 1 group, 67% of pelvic injuries were classified as stable fracture patterns and 33% were classified as unstable. In the level 2 group, 62% of pelvic injuries were classified as stable fracture patterns and 38% were classified as unstable. level 1

trauma code was not associated with odds of having an unstable fracture pattern (OR = 0.83, 95%CI: 0.48-1.41, $P = 0.485$). In the level 1 group with unstable pelvic injuries, 33% were discharged to home, 36% to a rehabilitation facility, and 32% died. In the level 2 group with unstable pelvic injuries, 65% were discharged to home, 31% to a rehabilitation facility, and 4% died. For those with unstable pelvic fractures ($n = 85$), assignment of a level 2 trauma code was associated with reduced odds of death (OR = 0.07, 95%CI: 0.01-0.35, $P = 0.001$) as compared to being discharged to home.

CONCLUSION: Trauma code level assignment is not correlated with severity of pelvic injury. Because an unstable pelvis can lead to hemodynamic instability, these injuries may be undertriaged.

Key words: Pelvic ring; Trauma code; Triage; Unstable pelvis; Abbreviated injury scale

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The assignment of trauma level is important as it dictates the urgency of response and the size of the responding team. Because of the high morbidity and mortality from pelvic fractures, especially unstable pelvic fractures, it is critical that these injuries be appropriately triaged once discovered or suspected. Our study did not show an association between the severity of the pelvic ring injury and the trauma code level. This lack of an association suggests patients with significant pelvic injuries may be under-triaged. These injuries may benefit from a more severe trauma code status to prevent any undue morbidity or mortality.

Haws BE, Wuertzer S, Raffield L, Lenchik L, Miller AN. Criteria for level 1 and level 2 trauma codes: Are pelvic ring injuries undertriaged? *World J Orthop* 2016; 7(8): 481-486 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/481.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.481>

INTRODUCTION

At all accredited trauma centers, patients are triaged into a level 1 or level 2 trauma code based on specific criteria. The composition of the trauma team and the urgency of the trauma response can then be tailored to meet the needs of the patient based on the trauma code level^[1]. Patients with the most serious injuries are designated a level 1 trauma, indicating a need for a larger trauma team and faster response time^[2]. The determination of trauma code criteria varies between hospitals and is based on elements such as physiologic data, types of injury, and mechanism of injury. Specific field criteria for a level 1 designation have been pre-

Table 1 Inclusion criteria for designation as a level 1 trauma code at the author's home institution

Level 1 adult trauma code criteria
Cardiac arrest (secondary to trauma)
Airway compromise, poor ventilation, or high potential for same (includes assisted ventilations, field intubation, referring facility intubation compromise, or inability to intubate)
Hypotension or shock (Systolic BP < 90 mmHg adults and age specific hypotension)
GCS ≤ 8 (Presumably due to trauma)
GSW to neck or torso (chest, back, abdomen, or groin), or extremity proximal to the elbow/knee
Receiving blood transfusion at any time prior to arrival to maintain vital signs (transfer patients, air transport)
Emergency physician discretion
Patients who develop any level 1 criteria during their
Emergency Department stay should be upgraded to a level 1 trauma code

GCS: Glasgow coma scale; GSW: Gunshot wound.

viously investigated. Criteria that are commonly used include hypotension in the field^[3], truncal gunshot wounds^[4], field Glasgow coma scale (GCS) < 15^[5], and age > 70^[6].

Pelvic ring injuries are associated with a high rate of morbidity, with a short-term complication rate ranging from 50%-80%^[7], and a high rate of mortality of over 8%^[8]. Our primary purpose was to determine if there is any association between trauma code level and the severity of pelvic ring injuries. Specifically, our hypothesis was that unstable pelvic ring injuries would have a higher association with level 1 trauma code status due to the hemodynamic compromise often seen with these severe injuries. Our secondary purpose was to compare post-hospital disposition associated with pelvis fractures for level 1 and 2 trauma codes to determine if the trauma code status correlated with different outcomes for these injuries.

MATERIALS AND METHODS

A retrospective review of all pelvic ring injuries at a single academic center from July 2010 to June 2013 was performed. The trauma registry was used to determine the trauma codes for each patient. Criteria from our home institution were used to define code status for each patient (Tables 1 and 2).

A single fellowship-trained orthopedic trauma surgeon retrospectively reviewed the computed tomography (CT) examinations of all patients and classified the injuries as stable or unstable using Abbreviated Injury Scale codes. This system was chosen because it is commonly used, is relatively simple, and has high reliability^[9]. For the purpose of this study, an intact posterior arch or an incomplete disruption of the posterior arch was considered stable and a complete disruption of the posterior arch was considered unstable. The pelvic injury classifications from the level 1 and level 2 groups were then compared. Patient disposition at discharge in level

Table 2 Inclusion criteria for designation as a level 2 trauma code at the author's home institution

Level 2 adult trauma code criteria
Heart rate < 50 or > 125 (> 100 if age > 65 yr)
Systolic BP < 110 mmHg (only if age > 65 yr)
Respiratory rate < 10 or > 29
GCS ≤ 10
Stab to neck or torso (chest, back, abdomen, or groin)
GSW head (without airway compromise)
Amputation proximal to knee or elbow
Two or more proximal long bone fractures
Crush injury to chest or pelvis
Paralysis/suspected spinal cord injury
Neurovascular compromise of an extremity
Age > 65 yr + anticoagulant use + significant trauma
Intubation at outside hospital (transfer patients)
Multisystem trauma on outside imaging (transfer patients)
Emergency physician discretion

GCS: Glasgow coma scale; GSW: Gunshot wound.

1 and level 2 groups were also compared.

Relationships between assignment of level 1 and level 2 trauma codes and pelvic injury stability and patient disposition at discharge were analyzed using logistic regression models in SAS 9.3.

RESULTS

There were 108 level 1 and 130 level 2 blunt trauma admissions. The mean age was 41 years, age range 15-90 years. In the level 1 group, 72/108 (67%) of pelvic injuries were stable and 36/108 (33%) were unstable. In the level 2 group, 81/130 (62%) of pelvic injuries were stable and 49/130 (38%) were unstable.

In the level 1 group with stable pelvic injuries, 27/72 (38%) were discharged to home, 28/72 (39%) to a rehabilitation facility, and 17/72 (24%) died. In the level 2 group with stable pelvic injuries, 63/81 (77%) were discharged to home, 14/81 (17%) to a rehabilitation facility, and 4/81 (5%) died. In the level 1 group with unstable pelvic injuries, 12/36 (33%) were discharged to home, 13/36 (36%) to a rehabilitation facility, and 11/36 (32%) died. In the level 2 group with unstable pelvic injuries, 32/49 (65%) were discharged to home, 15/49 (31%) to a rehabilitation facility, and 2/49 (4%) died (Table 3).

Assignment of a level 1 trauma code was not associated with odds of having an unstable fracture (OR = 0.83, 95%CI: 0.48-1.41, $P = 0.485$) ($n = 238$). There is an association between trauma code level and patient discharge status with higher rates of mortality in level 1 trauma activation (28 deaths in the level 1 group and 6 in the level 2 group). For all participants ($n = 238$), assignment of a level 2 trauma code was associated with reduced odds of death (OR = 0.09, 95%CI: 0.03-0.23, $P < 0.0001$) or being dispatched to a rehabilitation center (OR = 0.29, 95%CI: 0.16-0.53, $P < 0.0001$) as compared to being dispatched to home. For those with

Table 3 Numbers of unstable and stable pelvic fractures in level 1 compared to level 2 trauma code patients. Further stratified percentages of the outcomes of these patients (discharged home, discharged to rehabilitation facility, or died)

Trauma level	Stable or unstable	Discharged home	Discharged to rehabilitation facility	Died
Level 1	Stable	38%	39%	24%
108 patients	(72/108) 67%			
	Unstable	33%	36%	32%
	(36/108) 33%			
Level 2	Stable	77%	17%	5%
130 patients	(81/130) 62%			
	Unstable	65%	31%	4%
	(49/130) 38%			

stable pelvic fractures ($n = 153$), assignment of a level 2 trauma code was associated with reduced odds of death (OR = 0.10, 95%CI: 0.03-0.33, $P < 0.0001$) or being dispatched to a rehabilitation center (OR = 0.21, 95%CI: 0.10-0.47, $P < 0.0001$) as compared to being dispatched to home. For those with unstable pelvic fractures ($n = 85$), assignment of a level 2 trauma code was associated with reduced odds of death (OR = 0.07, 95%CI: 0.01-0.35, $P = 0.001$) as compared to being dispatched to home, with a trend towards reduced odds of being dispatched to a rehabilitation center as well (OR = 0.43, 95%CI: 0.16-1.17, $P = 0.099$).

DISCUSSION

The criteria used to determine trauma code status is not consistent across institutions. Although there are guidelines set by the American College of Surgeons (ACS), each institution modifies these guidelines for their own environment and patient population. Kouzminova *et al.*^[10], evaluated a two-tiered trauma activation system based on ACS field trauma center triage criteria. Their approach was effective in identifying patients with potentially serious injuries as all evaluated indicators of severe injury (including intubation, transfer to ICU or OR, and death) were significantly different between the level 1 and level 2 group ($P < 0.0001$)^[10]. Another study by Kaplan *et al.*^[11] compared a three-tiered system with a two-tiered system. This three-tiered system resulted in earlier involvement of the trauma service and decreased time in the emergency department. They also found that the amount of overtriage was decreased as defined by the number of patients who were not admitted to the hospital after Emergency Department evaluation. Eastes *et al.*^[12] evaluated patient outcomes in a tiered response system. They found that although this system led to a prolonged length of stay in the emergency department for those patients designated as a "partial trauma code", it did not compromise quality of patient care. These three studies all had their own criteria for defining a

level 1 trauma, however, many of these indications were similar, including hemodynamic instability, penetrating trauma, and altered consciousness. The use of other criteria such as breathing difficulty, focal neurological deficit, proximal extremity fracture, and paralysis varied among the three studies^[10-12]. Additionally, only one of the above studies included pelvic instability as an indicator for severe trauma^[12]. Although each of these studies had their own criteria for level 1 trauma activation, all were found to be effective at categorizing incoming traumas.

At our institution, pelvic ring instability is not included in the criteria for level 1 trauma code designation. Yoshihara *et al.*^[13] studied patients with unstable pelvic fractures and found an in-hospital mortality rate of 8.3%. Another study reported that patients with complex pelvic injuries have a mortality rate of 31.1%, and patients with pelvic fracture without concomitant soft tissue injury have a mortality rate of 10.8%^[14]. Due to the high morbidity and mortality from pelvic fractures, especially unstable pelvic fractures, the main purpose of this study was to determine if there is any association between trauma code level and the severity of pelvic ring injuries. In other words, the relationship of these injuries to adverse outcomes suggests a benefit for including them in level 1 criteria, leading to a larger trauma team and faster response time to manage these complex injuries.

An association between pelvic fractures and an increased injury severity score has been evaluated previously. Cordts Filho Rde *et al.*^[15] compared injury severity scores between trauma patients with a pelvic fracture and those without a pelvic fracture. They found that pelvic fractures were associated with a worse prognosis, including a 27.9% mortality rate in those with a pelvic fracture compared to a 1.8% mortality rate in those without a pelvic fracture. Our study is the first to evaluate the relationship between trauma code levels and pelvic fractures. Although previous studies have investigated patient disposition to validate the efficacy of their trauma criteria^[2,10,12], no study has directly examined how patient disposition compares between level 1 and level 2 trauma activations.

Our study did not show an association between the severity of the pelvic ring injury and the trauma code level. Because of the high morbidity and mortality from pelvic fractures, this lack of an association suggests patients with significant pelvic injuries may be under-triaged. Additionally, for the level 2 group with less severe injuries, patients with unstable pelvic injuries were less likely to be discharged home and more likely to be discharged to a rehabilitation facility compared to patients with stable pelvic injuries. Our data suggest that patients placed into the level 2 group with unstable pelvic injuries may have been under-triaged.

As expected, we found higher rates of mortality in level 1 trauma activations. Many of these patients

would have sustained significant injuries (*e.g.*, neurologic) that placed them into the level 1 trauma group, irrespective of their pelvis status. Our study shows the need to continually assess the trauma code criteria. For example, unstable pelvic fractures can rapidly lead to many of the criteria used by institutions for level 1 trauma designation, such as hemodynamic instability, but these criteria may not be present at the initial classification. In other words, because of the potential for morbidity and mortality, an unstable pelvic fracture should be used as a stand-alone criterion for categorizing a patient as a level 1 trauma.

Physical assessment of the pelvis should be performed in an emergency or prehospital setting to determine if a pelvic injury is likely present. This information could then be used to guide the trauma code level assignment. Important aspects of the evaluation include presence of pelvic pain or tenderness, pelvic deformity, and assessment of pelvic stability with gentle lateral compression (any gross motion should be considered a sign of instability). Shlamovitz *et al.*^[16] studied the probability that these parameters will accurately indicate the presence of a pelvic injury. They determined that the sensitivity and specificity of pelvic pain or tenderness in patients with GCS > 13 were 0.74 (95%CI: 0.64-0.82) and 0.97 (95%CI: 0.96-0.98), respectively for diagnosing any pelvic fractures, and 1.0 (95%CI: 0.85-1.0) and 0.93 (95%CI: 0.92-0.95), respectively for diagnosing mechanically unstable pelvic fractures. The sensitivity and specificity of the presence of pelvic deformity were 0.30 (95%CI: 0.22-0.39) and 0.98 (95%CI: 0.98-0.99), respectively for detection of any pelvic fracture and 0.55 (95%CI: 0.38-0.70) and 0.97 (95%CI: 0.96-0.98), respectively for detection of mechanically unstable pelvic fractures. Instability to pelvic ring compression had a sensitivity and specificity of 0.08 (95%CI: 0.04-0.14) and 0.99 (95%CI: 0.99-1.0), respectively, for detection of any pelvic fracture and 0.26 (95%CI: 0.15-0.43) and 0.999 (95%CI: 0.99-1.0), respectively, for detection of mechanically unstable pelvic fractures. While these findings are not highly sensitive, they are specific for pelvic fractures - particularly unstable fractures. Therefore, if any of these are found upon the prehospital assessment the likelihood of unstable pelvic fracture is high and could potentially be investigated for its utility as part of the criteria for level 1 trauma code assignment.

This study has some limitations, including the inherent flaws of any retrospective study. The use of a database relies on the quality of input, which may include inaccurate data or inaccurate data entry. Pelvic CT classification can be difficult^[17-19], however, we purposely chose a commonly used and reproducible scale to decrease errors in classification.

The assignment of trauma level is important as it dictates the urgency of response and the size of the

responding team. Because of the high correlation of internal injuries with unstable pelvic ring injuries, it is critical that these injuries be appropriately triaged, perhaps with a more severe trauma code status to prevent any undue morbidity or mortality.

COMMENTS

Background

At all accredited trauma centers, patients are triaged into a level 1 or level 2 trauma code based on specific criteria. The composition of the trauma team and the urgency of the trauma response are tailored to meet the needs of the patient based on the trauma code level. Patients with the most serious injuries are designated a level 1 trauma, indicating a need for a larger trauma team and faster response time. The determination of trauma code criteria varies between hospitals and is based on elements such as physiologic data, types of injury, and mechanism of injury. Because of the high morbidity and mortality from pelvic fractures, especially unstable pelvic fractures, it is thought that these injuries would likely be associated with a higher trauma code status.

Research frontiers

This study assessed the correlation between the severity of pelvic ring injury and the trauma code level. The authors found that patients with significant pelvic injuries may be under-triaged because of the lack of association with high trauma code status. This conclusion is supported by data analysis of patients with pelvic ring injuries compared to their trauma code level and disposition at discharge.

Innovations and breakthroughs

Data regarding the utility of using the severity of pelvic ring injury as criteria for higher trauma code level has not previously been assessed. This study describes a lack of association between the severity of the pelvic ring injury and the trauma code level. This suggests patients with significant pelvic injuries may be under-triaged potentially increasing the likelihood of morbidity or mortality.

Applications

Patients with suspected or confirmed unstable pelvic ring injury will benefit from higher trauma code status in order to allow for a more urgent response and therefore prevent undue morbidity and mortality. Inclusion of unstable pelvic ring injury in the criteria for level 1 traumas may lead to improved outcomes in this population.

Terminology

Trauma Code response in the Emergency Department is a standardized procedure used at trauma centers that dictates the initial management of trauma patients. This response may vary by timing and team size depending upon the perceived urgency indicated by the trauma code level. Upon arrival, trauma patients are evaluated clinically and with imaging by the general surgery team. After initial assessment, subspecialty services are consulted based upon the injuries found. General trauma surgeons do not typically manage pelvic fractures, so they would consult the orthopaedic surgery team in that circumstance. Assigning trauma code level determines which patients have the most severe injuries and therefore would benefit from the most rapid evaluation in order to allow for earliest intervention and best possible outcome.

Peer-review

The authors provide an interesting retrospective study on the relevance of pelvic injuries for the assignment of a trauma code level.

REFERENCES

- 1 **Lloyd DA**, Patterson M, Robson J, Phillips B. A stratified response system for the emergency management of the severely injured. *Ann R Coll Surg Engl* 2001; **83**: 15-20 [PMID: 11212442]
- 2 **Kohn MA**, Hammel JM, Bretz SW, Stangby A. Trauma team activation criteria as predictors of patient disposition from the

- emergency department. *Acad Emerg Med* 2004; **11**: 1-9 [PMID: 14709422 DOI: 10.1111/j.1553-2712.2004.tb01364.x]
- 3 **Franklin GA**, Boaz PW, Spain DA, Lukan JK, Carrillo EH, Richardson JD. Prehospital hypotension as a valid indicator of trauma team activation. *J Trauma* 2000; **48**: 1034-1037; discussion 1037-1039 [PMID: 10866247 DOI: 10.1097/00005373-200006000-00006]
- 4 **Sava J**, Alo K, Velmahos GC, Demetriades D. All patients with truncal gunshot wounds deserve trauma team activation. *J Trauma* 2002; **52**: 276-279 [PMID: 11834987 DOI: 10.1097/00005373-200202000-00012]
- 5 **Norwood SH**, McAuley CE, Berne JD, Vallina VL, Creath RG, McLarty J. A prehospital glasgow coma scale score <math>=> 14</math> accurately predicts the need for full trauma team activation and patient hospitalization after motor vehicle collisions. *J Trauma* 2002; **53**: 503-507 [PMID: 12352488 DOI: 10.1097/00005373-200209000-00018]
- 6 **Demetriades D**, Sava J, Alo K, Newton E, Velmahos GC, Murray JA, Belzberg H, Asensio JA, Berne TV. Old age as a criterion for trauma team activation. *J Trauma* 2001; **51**: 754-756; discussion 756-757 [PMID: 11586171 DOI: 10.1097/00005373-200110000-00022]
- 7 **Dunet B**, Tournier C, Billaud A, Lavoine N, Fabre T, Durandea A. Acetabular fracture: long-term follow-up and factors associated with secondary implantation of total hip arthroplasty. *Orthop Traumatol Surg Res* 2013; **99**: 281-290 [PMID: 23562708 DOI: 10.1016/j.otsr.2012.12.018]
- 8 **Poole GV**, Ward EF. Causes of mortality in patients with pelvic fractures. *Orthopedics* 1994; **17**: 691-696 [PMID: 7971521]
- 9 **Mitchell CS**, Cloeren M, Schwartz BS. Application of an injury surveillance system to injuries at an industrial facility. *Accid Anal Prev* 1993; **25**: 453-458 [PMID: 8357458]
- 10 **Kouzminova N**, Shatney C, Palm E, McCullough M, Sherck J. The efficacy of a two-tiered trauma activation system at a level I trauma center. *J Trauma* 2009; **67**: 829-833 [PMID: 19820592 DOI: 10.1097/TA.0b013e3181b57b6d]
- 11 **Kaplan LJ**, Santora TA, Blank-Reid CA, Trooskin SZ. Improved emergency department efficiency with a three-tier trauma triage system. *Injury* 1997; **28**: 449-453 [PMID: 9509085 DOI: 10.1016/S0020-1383(97)00088-0]
- 12 **Eastes LS**, Norton R, Brand D, Pearson S, Mullins RJ. Outcomes of patients using a tiered trauma response protocol. *J Trauma* 2001; **50**: 908-913 [PMID: 11371850 DOI: 10.1097/00005373-20010500-0-00022]
- 13 **Yoshihara H**, Yoneoka D. Demographic epidemiology of unstable pelvic fracture in the United States from 2000 to 2009: trends and in-hospital mortality. *J Trauma Acute Care Surg* 2014; **76**: 380-385 [PMID: 24398776 DOI: 10.1097/TA.0b013e3182ab0cde]
- 14 **Gänsslen A**, Pohlemann T, Paul C, Lobenhoffer P, Tscherne H. Epidemiology of pelvic ring injuries. *Injury* 1996; **27** Suppl 1: S-A13-S-A20 [PMID: 8762338 DOI: 10.1016/S0020-1383(96)90106-0]
- 15 **Cordts Filho Rde M**, Parreira JG, Perlingeiro JA, Soldá SC, Campos Td, Assef JC. Pelvic fractures as a marker of injury severity in trauma patients. *Rev Col Bras Cir* 2011; **38**: 310-316 [PMID: 22124641 DOI: 10.1590/S0100-69912011000500005]
- 16 **Shlamovitz GZ**, Mower WR, Bergman J, Chuang KR, Crisp J, Hardy D, Sargent M, Shroff SD, Snyder E, Morgan MT. How (un)useful is the pelvic ring stability examination in diagnosing mechanically unstable pelvic fractures in blunt trauma patients? *J Trauma* 2009; **66**: 815-820 [PMID: 19276759 DOI: 10.1097/TA.0b013e31817c96e1]
- 17 **Gabbe BJ**, Esser M, Bucknill A, Russ MK, Hofstee DJ, Cameron PA, Handley C, de Steiger RN. The imaging and classification of severe pelvic ring fractures: Experiences from two level I trauma centres. *Bone Joint J* 2013; **95-B**: 1396-1401 [PMID: 24078539 DOI: 10.1302/0301-620X.95B10.32134]
- 18 **Ringdal KG**, Skaga NO, Hestnes M, Steen PA, Roislien J, Rehn M, Røise O, Krüger AJ, Lossius HM. Abbreviated Injury Scale: not a reliable basis for summation of injury severity in trauma facilities?

Haws BE *et al.*. Pelvic injuries and trauma code criteria

Injury 2013; **44**: 691-699 [PMID: 22831922 DOI: 10.1016/j.injury.2012.06.032]

19 **MacKenzie EJ**, Shapiro S, Eastham JN. The Abbreviated Injury

Scale and Injury Severity Score. levels of inter- and intrarater reliability. *Med Care* 1985; **23**: 823-835 [PMID: 3925257 DOI: 10.1097/00005650-198506000-00008]

P- Reviewer: Herath SC, Pieske O **S- Editor:** Qiu S **L- Editor:** A
E- Editor: Wu HL



Retrospective Study

Femoro Patella Vialla patellofemoral arthroplasty: An independent assessment of outcomes at minimum 2-year follow-up

Mansur Halai, Andrew Ker, Iain Anthony, Graeme Holt, Bryn Jones, Mark Blyth

Mansur Halai, Andrew Ker, Iain Anthony, Bryn Jones, Mark Blyth, Department of Trauma and Orthopaedics, Glasgow Royal Infirmary, Glasgow G4 0SF, United Kingdom

Graeme Holt, Department of Trauma and Orthopaedics, University Hospital Crosshouse, Kilmarnock KA2 0BE, United Kingdom

Author contributions: Halai M conducted the study with the help of Ker A; Anthony I and Holt G performed the biostatistical analysis; Jones B and Blyth M conducted the study and supervised the entire project; all authors had read and approved the final version to be published.

Institutional review board statement: Not required. This study was performed as part our routine departmental audit process.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrolment.

Conflict-of-interest statement: All the authors have no conflicts of interest to declare.

Data sharing statement: We confirm that this article is original, is not under consideration by another journal and has not been previously published. We consent to *World J Orthop* using our data for sharing. Technical appendix, statistical code, and dataset available from the corresponding author at mansurhalai@googlemail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Mansur Halai, Specialty Registrar, Department of Trauma and Orthopaedics, Glasgow Royal Infirmary, Gatehouse Building, 84 Castle Street, Glasgow G4 0SF, United Kingdom. mansurhalai@gmail.com
 Telephone: +44-7790-508019

Received: February 27, 2016

Peer-review started: February 27, 2016

First decision: March 24, 2016

Revised: May 19, 2016

Accepted: June 1, 2016

Article in press: June 3, 2016

Published online: August 18, 2016

Abstract

AIM: To determine outcomes using the Femoro-Patella Vialla (FPV) arthroplasty and if there is an ideal patient for this implant.

METHODS: A total of 41 FPV patellofemoral joint replacements were performed in 31 patients (22 females, 9 males, mean age 65 years). Mean follow-up was 3.2 years (minimum 2 years). Radiographs were reviewed preoperatively and postoperatively. We assessed whether gender, age, previous surgery, patella atla or trochlear dysplasia influenced patient satisfaction or patient functional outcome.

RESULTS: The median Oxford Knee Score was 40 and the median Melbourne Patellofemoral Score was 21 postoperatively. Seventy-six percent of patients were satisfied, 10% unsure and 14% dissatisfied postoperatively. There was no radiological progression of tibiofemoral joint arthritis, using the Ahlback grading,

in any patient. One patient, who was diagnosed with rheumatoid arthritis postoperatively, underwent revision to total knee replacement. There were no intraoperative lateral releases and no implant failures. Gender, age, the presence of trochlear dysplasia, patella alta or bilateral surgery did not influence patient outcome. Previous surgery did not correlate with outcome.

CONCLUSION: In contrast to the current literature, the FPV shows promising early results. However, we cannot identify a subgroup of patients with superior outcomes.

Key words: Patellofemoral; Arthritis; Femoro-Patella Vialla; Outcomes; Arthroplasty

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We demonstrate good outcomes regarding the Femoro-Patella Vialla implant which recently has had poor outcomes reported. As it is a popular implant, we think this article is important as there is a paucity of literature concerning outcomes from independent centres. In addition, we are the first group to use a patellofemoral score as one of the outcome measures. However, we cannot identify a subgroup of patients with superior outcomes.

Halai M, Ker A, Anthony I, Holt G, Jones B, Blyth M. Femoro Patella Vialla patellofemoral arthroplasty: An independent assessment of outcomes at minimum 2-year follow-up. *World J Orthop* 2016; 7(8): 487-493 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/487.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.487>

INTRODUCTION

Patellofemoral arthroplasty (PFA) is a bone preserving procedure for the treatment of severe isolated patellofemoral arthritis. Its legacy dates back to Blazina's first report of PFA in 1979^[1]. Early designs, such as the Lubinus device, reported high failure rates^[2]. Since then, newer devices have been developed which more accurately mimic normal knee anatomy and patellar alignment. PFA is now a tibiofemoral joint-sparing alternative to traditional total knee arthroplasty in the treatment of patellofemoral arthritis.

The AVON (Stryker Howmedica Osteonics, Allendale, New Jersey) design was developed from the Kinemax plus (Stryker Howmedica Osteonics, New Jersey) which had a low rate of patellofemoral complications. The early results of this prosthesis from the originating centre have been promising^[3]. In another prospective review, good results were also experienced in 37 cases at 2 years^[4]. However, there have been mixed results in terms of revision rates at short term follow-up for patellofemoral arthroplasty in general, with rates of

between 3% and 15% quoted in the literature^[5].

Newer devices such as the Femoro-Patella Vialla (FPV, Wright Medical, United Kingdom) have more recently become available. Stated benefits include a broad trochlea with proximal extension, together with a sagittal curve that promotes superior patella tracking. The sulcus angle of the FPV is 140 degrees, which mimics the human trochlear anatomy more accurately, compared to the Avon which has an angle of 125 degrees^[6]. The trochlea is also designed to extend distally to the intercondylar notch, ensuring that the patella does not dislocate inferiorly in deep flexion. The patella features a faceted design with a longitudinal ridge which in theory contains the patella more readily in full extension. The footprint of the patella component is oval in shape, increasing patella contact area, in contrast to the AVON which has a medially offset dome.

There have been reports suggesting that the presence of preoperative trochlear dysplasia can be associated with superior outcomes after PFA^[7]. Another series have shown that patellofemoral arthritis associated with malalignment, such as patella alta, was the most common clinical presentation prior to PFA^[8]. Furthermore, Farr *et al*^[9] confirmed that the best outcome after PFA can be expected when the indication is trochlear dysplasia or patellar malalignment. All of these studies were not based on the FPV.

There are three independent outcome studies of the FPV in the literature, of which two of these report high rates of revision of 17%^[10,11]. We are not aware of any studies looking at the effects of pre-existing patella alta, trochlear dysplasia or bilateral disease on outcome of the FPV specifically. In addition, none of the published studies have used a validated patellofemoral score as one of their outcome measures. We report early outcomes of the FPV in 41 consecutive knees with a minimum follow up of 2 years.

MATERIALS AND METHODS

Forty-four consecutive FPV PFAs were performed at a single tertiary centre between November 2007 and November 2011. One patient died from unrelated causes and another patient, who had bilateral FPVs implanted, was lost to follow up. The patient lost to follow-up had a normal postoperative recovery and satisfactory radiographs, with no revision surgery documented in their case-notes.

This left 41 FPV procedures in 31 patients producing a 94% follow-up rate. There were 22 females and 9 males. There were 11 patients (22 FPVs) who had bilateral replacements as staged procedures. The mean age of the cohort was 65 years (range 41-81). The mean follow-up was 3.2 years with a minimum of 2-year follow-up for all patients. The causes of the patellofemoral arthritis were as follows: Osteoarthritis (39 cases, 95%) and trauma (2 cases, 5%).

Patients were considered for surgery if they had

Table 1 Previous surgery in 41 knees

Previous surgery	No. of knees (% of total)
Arthroscopy	3 (7)
Tibial tuberosity transfer	2 (5)
Medial patellofemoral ligament reconstruction	2 (5)
No intervention	34 (83)
Total	41 (100)

disabling knee pain, Outerbridge grade 4 patellofemoral arthritis and normal medial and lateral knee compartments on weight-bearing radiographs^[12]. The preoperative diagnosis was isolated severe patellofemoral arthritis in all cases. Diagnosis was based on a combination of clinical, radiological and, where available, arthroscopic findings. Previous surgery was documented and summarised in Table 1.

Each patient had a weight-bearing anteroposterior, lateral radiograph and skyline radiograph of their affected knee preoperatively (Figure 1). The presence of a dysplastic trochlea was evaluated on preoperative radiographs, including a true lateral. This was scored independently by two of the authors. Trochlear dysplasia was identified where there was a crossing sign and a sulcus angle greater than 145° as has been previously described^[13]. The presence of patella alta was also documented from the lateral preoperative radiographs using the Insall-Salvati ratio^[14]. A ratio of greater than 1.2 was taken to be indicative of patella alta.

All operations were performed by, or under direct supervision of, the two senior authors. A medial parapatellar approach was adopted in all cases under pneumatic tourniquet control. All patients had intravenous antibiotics at induction as per local microbiology policy. Palacos R and G cement was used in all cases. No lateral releases were performed. The mean tourniquet time was 49 min. No patients required a blood transfusion postoperatively. The median time for discharge for all patients was at day 3 postoperatively.

Patients were followed in our Outcomes Assessment clinic run by independent nurse practitioners. We performed a retrospective audit of case-notes and radiographs. Patient factors such as preoperative diagnosis and a history of previous surgery or trauma were noted. Functional outcome was assessed at scheduled appointments. These consisted of a preoperative visit and a 3 mo postoperative visit. Thereafter patients were reviewed on a yearly basis. The mean follow-up at the latest appointment was 3.2 years (range 24–58 mo). Patient reported outcome measures included the Oxford Knee Score (OKS) and the validated Melbourne Patellofemoral Score^[15,16]. Patient satisfaction with the outcome of the surgery was also documented using a simple 5 point question. The patient was asked in writing, at latest follow-up, to grade their satisfaction postoperatively as: Very satisfied, satisfied, unsure, dissatisfied or very dissatisfied. Radiographs were reviewed postoperatively for the development of

Table 2 Effect of different patient characteristics on outcome

Patient factor	Category	n	Median OKS (Q1, Q3)	P value	Mean Melbourne Score (SD)	P value
Sex	Male	12	42 (38, 46)	0.28	21.3 (4.7)	0.31
	Female	29	40 (37, 42)		19.1 (6.4)	
Trochlear dysplasia	Non-dysplastic	10	41 (36, 43)	0.95	20.0 (5.7)	0.67
	Dysplastic	31	41 (38, 43)		19.0 (7.1)	
Patella alta	Yes	21	41 (37, 42)	0.56	19.3 (6.4)	0.65
	No	20	40 (36, 44)		20.2 (5.6)	
Uni- or bi-lateral	Unilateral	19	41 (37, 42)	0.83	19.8 (5.6)	0.97
	Bilateral	22	41 (37, 43)		19.7 (6.4)	
Previous surgery	Yes	10	40 (37, 42)	0.70	22.0 (5.0)	0.28
	No	31	41 (37, 43)		19.0 (6.1)	

OKS: Oxford Knee Score.

tibiofemoral arthritis using the Ahlback grading^[17]. Complications were determined at postoperative clinic visits and from the case-notes. The data presented was collected retrospectively and analysed as part of a routine audit of our clinical practice.

Statistical analysis

All data was analysed using SigmaPlot vs11.0 (Systat Software Inc). Parametric data (Melbourne Score) was analysed using *t* test and non-parametric data (OKS) was analysed using Mann-Whitney test. Pearson's correlation was used to determine linear correlation between variables. *P* value less than 0.05 was considered significant for all tests. The statistical methods of this study were conducted by the biostatistician Iain Anthony of the Glasgow Royal Infirmary.

RESULTS

The median postoperative OKS and Melbourne scores were 40 and 21 respectively at latest follow-up. Thirty-eight percent of patients were very satisfied, 38% satisfied, 10% unsure and 14% dissatisfied with their final result. There were no patients who were "very dissatisfied". The results are summarised with respect to different patient characteristics in Table 2. Patient factors (gender, the presence of trochlear dysplasia or patella alta, or if bilateral surgery was performed) did not impact on clinical outcome scores. Previous surgery had no significant effect on clinical outcome. No significant correlation was found between age and OKS or Melbourne score ($P = 0.162$, $r = 0.273$ and $P = 0.278$, $r = -0.173$ respectively).

Two patients had superficial wound infections that were diagnosed and treated with a course of oral antibiotics in the community within 2 wk of discharge. Both patients went on to have favourable outcomes and were satisfied. There were no deep infections to date and there have been no infections that have required operative attention. We report no mechanical failures of the FPV prosthesis and there have been no

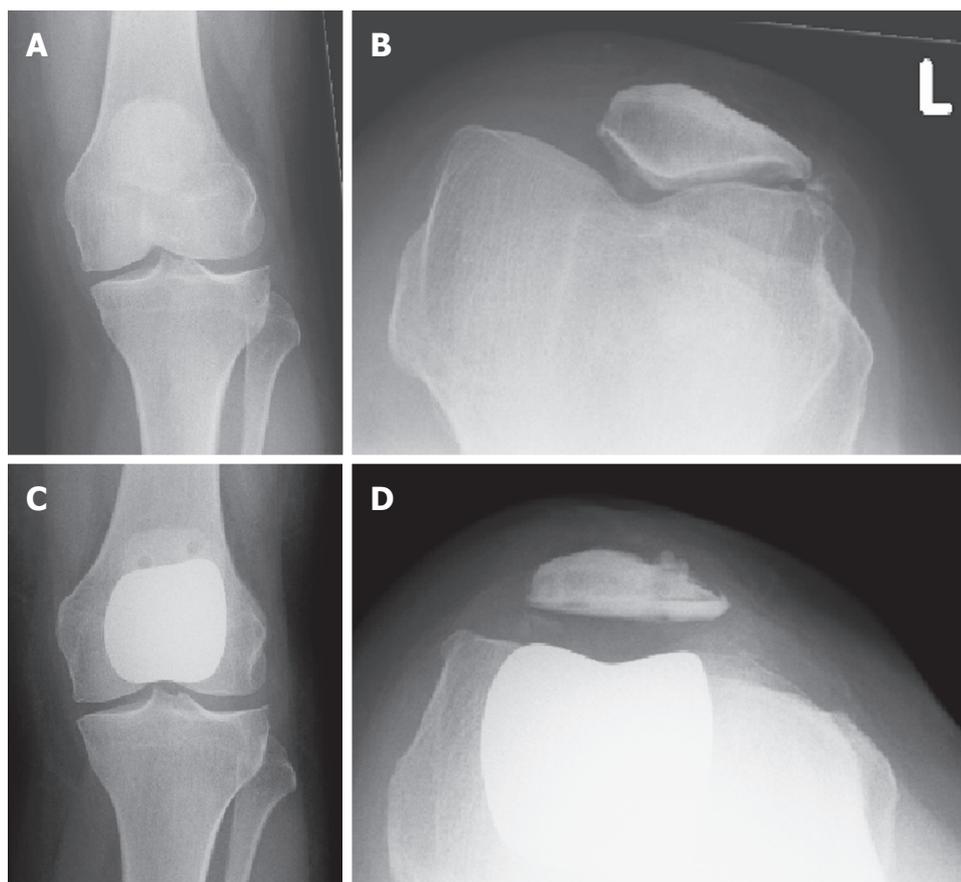


Figure 1 Preoperative and postoperative radiographs using the Femero-Patella Vialla implant. Preoperative (A) weight-bearing anteroposterior, (B) skyline radiographs in a 60-year-old woman with severe patellofemoral degeneration and subluxation. Postoperative weight-bearing radiographs show satisfactory placement of the prosthesis on the (C) anteroposterior, and (D) skyline views of the same patient at 2 years.

periprosthetic fractures. The complications are included in Table 3.

One patient was diagnosed with seronegative rheumatoid arthritis subsequent to her FPV replacement and was revised to a total knee replacement (TKR) at 6 mo following her index procedure. This represents a 97.6% survival at minimum 2 years of follow-up.

At latest follow-up, there was no progression of arthritis of the tibiofemoral joint using the Ahlback grading in any case. In addition there was no medial or lateral tilt of the patella postoperatively and no lateral releases have been performed postoperatively.

DISCUSSION

Our study shows that good results can be achieved in the short term with the FPV patellofemoral joint replacement. The high Oxford and Melbourne scores observed are reflected in a 78% patient satisfaction rate (satisfied or very satisfied). The procedure compares favourably to TKR with a mean tourniquet time of 49 min, no blood transfusions, a mean length of stay of 3 d and an OKS of 40, at a minimum of 2 years follow-up.

The philosophy behind PFR is theoretically appealing for selected patients with isolated patellofemoral arthritis

whom have failed with non-operative therapies. The PFR spares the tibiofemoral joint, with both anterior and posterior cruciate ligaments and menisci, and therefore allows for more natural kinematics, leaving more bone stock for revision surgery^[18].

Anatomical patellofemoral abnormalities such as trochlear dysplasia and patella alta are increasingly recognised as the underlying cause of the later development of patellofemoral osteoarthritis. Farr *et al*^[9] concluded in their study that better outcomes after PFR were seen in patients with trochlear dysplasia. Williams *et al*^[10] has recently explored the relationship between trochlear dysplasia and FPV outcomes. They reported 7 revisions in their cohort of 48 knees at 2 years follow-up. Trochlear dysplasia was associated with a significantly lower rate of revision and a lower incidence of persistent pain in their cohort. In our study, it was interesting that over 80% of patients had a dysplastic trochlea according to Dejour's classification, with over half displaying patella alta. Patellofemoral abnormalities were therefore present in the majority of the patients undergoing surgery in our series, although their presence had neither a positive or negative effect on clinical outcome.

Interestingly, despite the relative paucity of published

Table 3 A comparison of our results with those previously published for patellofemoral arthroplasty and total knee replacement for isolated patellofemoral arthritis

Ref.	Implant	Number knees/patients	Mean age (yr)	Mean follow-up (yr)	OKS	Melbourne Score	Patient satisfaction	Trochlear dysplasia	Complications	Further operations
Dalury ^[23]	TKR	33/25	70	5.2	NR	NR	100%	NR	NR	0
Ackroyd <i>et al</i> ^[3]	AVON	109/85	68	5.0	39	25	80%	NR	4 superficial infections 2 stiffness	4 (4.2%) conversions to TKR
Starks <i>et al</i> ^[4]	AVON	37/29	66	2.0	39	28	86%	NR	1 patella fracture 1 patella resurfacing	1 (2.7%) patella resurfacing
Al-Hadithy <i>et al</i> ^[22]	FPV	49/41	62	3.0	38	NR	NR	NR	1 scar pain	3 (6%); 2 (4%) to TKR
Williams <i>et al</i> ^[10]	FPV	48/48	63	2.1	NR	NR	NR	Trochlear dysplasia associated with less revision	10 persistent pain 1 infection, 1 fracture, 1 hypertrophic scar	7 (15%); 5 to TKR
The present report	FPV	41/31	65	3.2	40	21	78%	84% of cases had trochlear dysplasia preoperatively No difference in outcomes	2 superficial infections: Treated with oral antibiotics	1 (2%) conversion to TKR. No lateral releases

NR: Not recorded; OKS: Oxford Knee Score; FPV: Femoro-Patella Vialla; TKR: Total knee replacement.

results, the FPV is the second most used prosthesis for PFR in England and Wales, with the 10th annual National Joint Registry report stating that the FPV was used in approximately 20% of all PFRs performed in 2012 (National Joint Registry for England and Wales^[19]). Revision rates for PFR are reported in the National Joint Registry to be 6 times higher than that of primary cemented TKR. Persistent pain is the main cause of revision according to the recent registry data. If all FPVs are considered, the registry calculates a 6.4% (range 4.9%-8.2%) Kaplan-Meier estimate of the cumulative percentage probability of first revision (95%CI) at 3 years. Our 3-year data shows a FPV revision rate of 2%.

Baker *et al*^[20] examined the National Joint Registry and concluded that persistent unexplained pain was the principal reason for early revision following PFR, and that revisions usually occurred within the first 2 years. They suggested that patient selection was extremely important, and that PFR surgery should be concentrated in specialist centres. Therefore, we are encouraged by our 2% rate of revision at 3 years.

As with all partial knee replacements, ease of revision undoubtedly affects the rate of early failure. Faced with the unhappy patient, surgeons are potentially more likely to offer conversion to a TKR, as this can usually be achieved with straightforward surgery using primary TKR implants. However there is evidence that revision of partial joint replacements for unexplained pain does not give the pain relief experienced by those who are revised when a cause for failure has been identified^[21]. Our low early revision rate might be explained by our reluctance to offer revision surgery to

patients dissatisfied with the results of their procedure unless an identified cause for the dissatisfaction could be found.

A further apprehension about PFR is the advancement of osteoarthritis in the tibiofemoral articulation. In our series, there was no progression of tibiofemoral osteoarthritis at latest follow-up. Patient selection is critical and our success may be explained by our selection of patients with underlying trochlear dysplasia as a cause of their patellofemoral arthritis in the vast majority of cases. These patients are perhaps less likely to develop failure of the remainder of the knee over time, than patients whose patellofemoral arthritis develops as part of a more generalised degenerative process. Tibiofemoral osteoarthritis is not always easily identified either preoperatively. Magnetic resonance imaging (MRI) has been used to identify occult degenerative changes in the tibiofemoral articulation by the presence of subchondral cysts^[7]. We did not routinely use MRI to screen for occult tibiofemoral arthritis in our patients and our good early results question the requirement for this expensive screening investigation.

The main weakness of our study is a lack of pre-operative scores. In addition, this is a retrospective series with relatively small numbers and we do not have long-term follow-up yet. Nevertheless, our mean follow-up of 3.2 years is the longest for this implant in the literature. We specifically did not use a validated satisfaction score, such as the Western Ontario and McMaster Universities Osteoarthritis Index or SF12, for simplicity as we decided that the outcome measure process had to be streamlined. The satisfaction grading

that was used in this study is used for all research projects from our institution.

Table 3 shows that our postoperative results are comparable to those previously published for patellofemoral arthroplasty and for TKR for isolated patellofemoral arthritis. There is one published report by Al-Hadithy *et al*^[22], and they report similar satisfactory FPV outcomes with OKSs of 38 at 3 years. They reported 2 revisions, which were attributed to poor patient selection. Indeed, the one conversion to TKR in our series was due to a subsequent diagnosis of rheumatoid arthritis and this could also be retrospectively attributed to poor patient selection.

In conclusion, our early results suggest that the FPV patellofemoral joint replacement is a good alternative to TKR in the surgical management of advanced isolated patellofemoral osteoarthritis. However, we are unable to identify a subgroup of patients with superior outcomes, however do not recommend this procedure in patients suffering from rheumatoid arthritis. Further research is required to see if these initial promising results are maintained at longer term follow-up.

COMMENTS

Background

The knee joint has three compartments: Medial, lateral and patellofemoral. Some patients have isolated patellofemoral arthritis and therefore a novel "patellofemoral arthroplasty" is a treatment option to replace this compartment only, sparing the rest of the native knee joint.

Research frontiers

These patellofemoral replacements are new and there is limited outcome evidence on this particular implant: The Femoro Patella Vialla (FPV) arthroplasty.

Innovations and breakthroughs

In contrast to the current literature, the FPV shows promising early results at 2 years in this study. However, the authors cannot identify a subgroup of patients with superior outcomes. The authors do not recommend performing this procedure on patients with a history of inflammatory arthritis.

Applications

These encouraging outcomes are some of the first published outside the designing centre. The authors await longer outcome studies.

Terminology

"Patellofemoral" means the joint of the femur and patella (kneecap).

Peer-review

The authors have submitted a clinical analysis of the efficacy of using FPV patellofemoral joint replacement as a good alternative to total knee replacement in the surgical management of advanced isolated patellofemoral osteoarthritis. The authors have a relatively good selection of patients in the clinical trial (41 replacements in 31 patients) with radiographic observations and lysholm scoring techniques. The paper is well written and will be of interest to readers.

REFERENCES

- 1 **Blazina ME**, Fox JM, Del Pizzo W, Broukhim B, Ivey FM. Patellofemoral replacement. 1979. *Clin Orthop Relat Res* 2005; **(436)**: 3-6 [PMID: 15995413 DOI: 10.1097/00003086-197910000-00017]
- 2 **Tauro B**, Ackroyd CE, Newman JH, Shah NA. The Lubinus patellofemoral arthroplasty. A five- to ten-year prospective study. *J Bone Joint Surg Br* 2001; **83**: 696-701 [PMID: 11476308]
- 3 **Ackroyd CE**, Newman JH, Evans R, Eldridge JD, Joslin CC. The Avon patellofemoral arthroplasty: five-year survivorship and functional results. *J Bone Joint Surg Br* 2007; **89**: 310-315 [PMID: 17356140 DOI: 10.1302/0301-620X.89B3.18062]
- 4 **Starks I**, Roberts S, White SH. The Avon patellofemoral joint replacement: independent assessment of early functional outcomes. *J Bone Joint Surg Br* 2009; **91**: 1579-1582 [PMID: 19949120 DOI: 10.1302/0301-620X.91B12.23018]
- 5 **Sarda PK**, Shetty A, Maheswaran SS. Medium term results of Avon patellofemoral joint replacement. *Indian J Orthop* 2011; **45**: 439-444 [PMID: 21886926 DOI: 10.4103/0019-5413.83761]
- 6 **Davies AP**, Costa ML, Shepstone L, Glasgow MM, Donell S. The sulcus angle and malalignment of the extensor mechanism of the knee. *J Bone Joint Surg Br* 2000; **82**: 1162-1166 [PMID: 11132279 DOI: 10.1302/0301-620X.82B8.10833]
- 7 **Nicol SG**, Loveridge JM, Weale AE, Ackroyd CE, Newman JH. Arthritis progression after patellofemoral joint replacement. *Knee* 2006; **13**: 290-295 [PMID: 16769215 DOI: 10.1016/j.knee.2006.04.005]
- 8 **Cartier P**, Sanouiller JL, Grelsamer R. Patellofemoral arthroplasty. 2-12-year follow-up study. *J Arthroplasty* 1990; **5**: 49-55 [PMID: 2319248 DOI: 10.1016/S0883-5403(06)80009-4]
- 9 **Farr J**, Barrett D. Optimizing patellofemoral arthroplasty. *Knee* 2008; **15**: 339-347 [PMID: 18722775 DOI: 10.1016/j.knee.2008.05.008]
- 10 **Williams DP**, Pandit HG, Athanasou NA, Murray DW, Gibbons CL. Early revisions of the Femoro-Patella Vialla joint replacement. *Bone Joint J* 2013; **95-B**: 793-797 [PMID: 23723274 DOI: 10.1302/0301-620X.95B6.31355]
- 11 **Davies AP**. High early revision rate with the FPV patello-femoral unicompartmental arthroplasty. *Knee* 2013; **20**: 482-484 [PMID: 23953660 DOI: 10.1016/j.knee.2013.07.005]
- 12 **Outerbridge RE**. The etiology of chondromalacia patellae. 1961. *Clin Orthop Relat Res* 2001; **(389)**: 5-8 [PMID: 11501822]
- 13 **Dejour H**, Walch G, Nove-Josserand L, Guier C. Factors of patellar instability: an anatomic radiographic study. *Knee Surg Sports Traumatol Arthrosc* 1994; **2**: 19-26 [PMID: 7584171 DOI: 10.1007/BF01552649]
- 14 **Berg EE**, Mason SL, Lucas MJ. Patellar height ratios. A comparison of four measurement methods. *Am J Sports Med* 1996; **24**: 218-221 [PMID: 8775124 DOI: 10.1177/036354659602400218]
- 15 **Dawson J**, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br* 1998; **80**: 63-69 [PMID: 9460955 DOI: 10.1302/0301-620X.80B1.7859]
- 16 **Feller JA**, Bartlett RJ, Lang DM. Patellar resurfacing versus retention in total knee arthroplasty. *J Bone Joint Surg Br* 1996; **78**: 226-228 [PMID: 8666630]
- 17 **Ahlbäck S**. Osteoarthritis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968; **Suppl 277**: 7-27772 [PMID: 5706059]
- 18 **Hollingshurst D**, Stoney J, Ward T, Pandit H, Beard D, Murray DW. In vivo sagittal plane kinematics of the Avon patellofemoral arthroplasty. *J Arthroplasty* 2007; **22**: 117-123 [PMID: 17197318 DOI: 10.1016/j.arth.2006.02.160]
- 19 National Joint Registry for England and Wales 10th Report 2013. Available from: URL: <http://www.njrcentre.org.uk>
- 20 **Baker PN**, Refaie R, Gregg P, Deehan D. Revision following patellofemoral arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 2047-2053 [PMID: 22228375 DOI: 10.1007/s00167-011-1842-0]
- 21 **Kerens B**, Boonen B, Schotanus MG, Lacroix H, Emans PJ, Kort NP. Revision from unicompartmental to total knee replacement: the clinical outcome depends on reason for revision. *Bone Joint J* 2013; **95-B**: 1204-1208 [PMID: 23997133 DOI: 10.1302/0301-620X.95B.9.31085]
- 22 **Al-Hadithy N**, Patel R, Navadgi B, Deo S, Hollingshurst D, Satish V. Mid-term results of the FPV patellofemoral joint replacement.

Knee 2014; **21**: 138-141 [PMID: 24579096 DOI: 10.1016/j.knee.2013.08.010]

23 **Dalury DF**. Total knee replacement for patellofemoral disease. *J Knee Surg* 2005; **18**: 274-277 [PMID: 16262008]

P- Reviewer: Cartmell S, Malik H **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Wu HL



Retrospective Study

Condensing osteitis of the clavicle in children

Antonio Andreacchio, Lorenza Marengo, Federico Canavese

Antonio Andreacchio, Lorenza Marengo, Department of Pediatric Orthopedic Surgery, Regina Margherita Children's Hospital, 10100 Torino, Italy

Federico Canavese, Department of Pediatric Surgery, University Hospital Estaing, 63003 Clermont Ferrand, France

Author contributions: Andreacchio A and Canavese F designed and performed the research and wrote the paper; Marengo L contributed to the analysis and revised the text.

Institutional review board statement: The study was reviewed and approved by the local Institutional Review Board (Comité de Protection des Personnes Sud-Est 6; ref. 2016/CE01).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Federico Canavese, MD, PhD, Professor of Pediatric Orthopedic Surgery, Department of Pediatric Surgery, University Hospital Estaing, 1 place Lucie et Raymond Aubrac, 63003 Clermont Ferrand, France. canavese_federico@yahoo.fr
Telephone: +33-4-73750293
Fax: +33-4-73750291

Received: February 23, 2016

Peer-review started: February 25, 2016

First decision: April 15, 2016

Revised: May 13, 2016

Accepted: June 1, 2016

Article in press: June 3, 2016

Published online: August 18, 2016

Abstract

AIM: To confirm the rarity of this disorder and then to evaluate the effects of antibiotic treatment alone and assess whether this could produce a complete remission of symptoms in children and adolescents.

METHODS: We made a retrospective review of all cases of condensing osteitis of the clavicle in children and adolescents between January 2007 and January 2016. Outpatient and inpatient medical records, with radiographs, magnetic resonance imaging, triphasic bone scan and computed tomography scans were retrospectively reviewed. All the patients underwent biopsy of the affected clavicle and were treated with intra venous (IV) antibiotics followed by oral antibiotics.

RESULTS: Seven cases of condensing osteitis of the clavicle were identified. All the patients presented with swelling of the medial end of the clavicle, and 5 out of 7 reported persisting pain. The patients' mean age at presentation was 11.5 years (range 10.5-13). Biopsy confirmed the diagnosis in all cases. All the patients completed the treatment with IV and oral antibiotics. At last follow-up visit none of the patients complained of residual pain; all had a clinically evident reduction in the swelling of the medial end of the affected clavicle. The mean follow-up was 4 years (range 2-7).

CONCLUSION: Our findings show that condensing osteitis of the clavicle is a rare condition. Biopsy is needed to confirm diagnosis. The condition should be managed with IV and oral antibiotics. Aggressive

surgery should be avoided.

Key words: Condensing osteitis; Clavicle; Children; Benign tumor; Infection

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Condensing osteitis of the clavicle is a rare benign disorder. It is characterized by pain and swelling at the medial end of the clavicle, with increased radiodensity. Neither the etiology of this rare condition nor its treatment options are completely clarified. Condensing osteitis of the clavicle in children and adolescents should be recognized promptly. Biopsy is needed to confirm diagnosis. Once diagnosis is made, the condition should be treated by parenteral and oral antibiotic therapy, and aggressive surgery should be avoided.

Andreaschio A, Marengo L, Canavese F. Condensing osteitis of the clavicle in children. *World J Orthop* 2016; 7(8): 494-500 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/494.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.494>

INTRODUCTION

Brower *et al*^[1] first described condensing osteitis of the clavicle in 1974. The condition was originally described as a syndrome causing pain and swelling over the medial end of the clavicle with increased radiographic density (sclerosis).

Since its first description, few cases of this condition have been described in the English-language literature^[2-6]. Some authors consider it as an infective disease - a low-grade chronic osteomyelitis - while others suggest it could be a benign neoplastic process^[4,7-9]. However, the etiology of this condition and its best treatment options still remain to be determined^[2,5,7,10,11].

Although some cases of spontaneous remission have been observed, the disease often requires treatment. Conservative and surgical options have been described. A number of other different treatments have been recommended over the years, including antibiotic treatment, radiotherapy, chemotherapy, injection of corticosteroids or surgical resection of the medial end of the clavicle in refractory cases^[4-6]. However, the etiology of this rare condition and its best form of treatment are still unknown^[2,4,11-14].

This study set out to confirm the rarity of this pathology and to assess the outcome of patients treated by parenteral [intra venous (IV)] and oral antibiotic therapy. A review of the literature was also made.

MATERIALS AND METHODS

We made a retrospective review of the archive of clinical

records identifying all cases of condensing osteitis of the clavicle diagnosed at our children's hospital from January 2007 to January 2016. Informed consent was obtained. Outpatient and inpatient medical records were reviewed, and we collected the following information for each of the patients: Sex, age at time of diagnosis, side involved, symptomatic picture at presentation, blood tests, type and length of antibiotic therapy, complications and outcome (Table 1).

Standard antero-posterior (AP) radiographs of the clavicle, magnetic resonance imaging (MRI), triphasic bone scan (TBS) and computed tomography (CT) scans were also retrospectively reviewed.

All the patients underwent biopsy of the affected clavicle.

Literature review

A search of the Medline database from 1950 to 2016 was made to identify papers related to condensing osteitis of the clavicle in children, adolescents and adults.

As recommended by the Cochrane Handbook of Systematic reviews^[15], a variety of search terms ("condensing", "osteitis", "clavicle" and "children") were used, including a combination of index and free-text terms.

Abstracts were screened, and relevant full texts of articles retrieved for further review. Reference sections of papers were also scrutinized to identify additional literature. All levels of evidence were included.

We retrieved 23 studies reporting a total of 51 patients (52 clavicles) with condensing osteitis of the clavicle. A total of 58 patients (59 clavicles), including our cases, were identified (Table 2).

RESULTS

Seven cases of condensing osteitis were identified during study period (Table 1). There were 5 girls and 2 boys. The mean age of the patients at the time of diagnosis was 11.5 years (range 10.5-13 years). The right side was involved in all cases. All the patients presented with swelling of the medial end of the clavicle. Five out of 7 patients complained of pain worsened by finger pressure at the level of the sterno-clavicular joint.

The swelling was investigated in all the patients, with a standard AP radiograph of the affected clavicle, MRI and TBS. Five out of 7 patients also underwent a CT scan of the affected clavicle.

AP radiographs of the right clavicle (7/7 patients) showed expansion of the medial end of the clavicle, with signs of bone resorption and apposition in all cases (Figure 1).

MRI (7/7 patients) showed bone signal alterations of the medial end of the affected clavicle, and edema of the surrounding soft tissues in all cases.

CT scans (5/7 patients) showed expansion of the

Table 1 Patient demographics										
Patient	Age (yr)	Side	Gender	Symptoms	Biopsy	Antibiotic 1	Antibiotic 2	Evolution	Complications	
1	10.5	Right	Male	Pain and discomfort in the sterno-clavicular joint Swelling	Yes	Teicoplanin Rifampin 8 wk		Remission	-	
2	11.2	Right	Male	Pain and discomfort in the sterno-clavicular joint Swelling	Yes	Teicoplanin Amoxicillin/ clavulanic acid 17 d	Rifampin Trimethoprim- sulfamethoxazole 13 d	Remission	-	
3	11.2	Right	Male	Pain and discomfort in the sterno-clavicular joint Swelling	Yes	Teicoplanin Amoxicillin/ clavulanic acid 17 d	Rifampin Trimethoprim- sulfamethoxazole 13 d	Remission	-	
4	12.1	Right	Female	Pain and discomfort in the sterno-clavicular joint Swelling	Yes	Teicoplanin Amoxicillin/ clavulanic acid 17 d	Rifampin Trimethoprim- sulfamethoxazole 13 d	Remission	-	
5	12.4	Right	Male	Pain and discomfort in the sterno-clavicular joint Swelling	Yes	Teicoplanin Rifampin 8 wk		Remission	-	
6	11.5	Right	Female	Swelling	Yes	Teicoplanin Amoxicillin/ clavulanic acid 13 d	Azithromycin 5 d Rifampin Amoxicillin/clavulanic acid 10 wk	Remission	Adverse effect with Teicoplanin	
7	13	Right	Male	Swelling	Yes	Teicoplanin Amoxicillin/ clavulanic acid 17 d	Rifampin Trimethoprim- sulfamethoxazole 13 d	Recurrence of pain	-	



Figure 1 Radiograph of a patient with condensing osteitis showing expansion of the medial end of right clavicle and remodeling of bone.

medial half of the clavicle with no evidence of infection or tumor in all cases (Figure 2).

TBS (7/7 patients) was characterized by a strong hyperfixation of the medial half of the affected clavicle in all cases (Figure 3).

Results of blood tests, including inflammatory markers, were normal in all but 2 cases, in which C-reactive protein level was slightly increased (22.3 mg/dL), reverting to its normal range (< 10 mg/dL) after 4 d of IV antibiotic therapy.

All the patients underwent an incisional biopsy taken from the medial end of the affected clavicle for histology and cultures. Tissues cultures were negative, while histological results reflected a chronic inflammatory

process in all the patients. These features were compatible with the diagnosis of condensing osteitis.

Antibiotic treatment

In agreement with Jones' hypothesis of an infectious etiology^[6], all the patients received teicoplanin (10 mg/kg every 12 h for a total of 3 doses, followed by 10 mg/kg every 24 h) combined with another type of antibiotic. Two patients received teicoplanin combined with rifampin (300 mg every 12 h) for 56 d. Five patients received teicoplanin combined with amoxicillin/clavulanic acid (1 g every 6 h) for 17 d. The treatment choice was decided by the pediatric infectiologist.

At discharge, all the patients discontinued the IV treatment and started oral rifampin (600 mg every 24 h) and trimethoprim-sulfamethoxazole (80 mg + 200 mg every 12 h) for 13 d.

One patient developed an adverse drug reaction to teicoplanin after 13 d of treatment. The treatment with teicoplanin and amoxicillin was discontinued, and was replaced by azithromycin (300 mg every 12 h) for 5 d and amoxicillin/clavulanic acid (680 mg + 97 mg every 8 h) for 70 d and rifampin (450 mg every 24 h) for 65 d.

All the patients responded well to antibiotic therapy, and showed complete remission of pain and an initial decrease in the swelling.

After 5 mo of therapy one patient experienced a recurrence of pain at the same site. The patient was treated with amoxicillin/clavulanic acid for 14 d with complete remission of symptoms.

Table 2 Review of the literature		
Ref.	Number of cases	Symptoms
Brower <i>et al</i> ^[1]	1	Pain
Teates <i>et al</i> ^[12]	2	
Simpson ^[3,5-7,10]	1	Limited ROM
Duro ^[3,5-7,10]	2	
Appell <i>et al</i> ^[2]	7	
Weiner ^[3,5,10]	1	Pain
Franquet ^[3,5,10]	2	Pain (related to work)
Cone ^[3,5,10]	1	Pain (worsening)
Kruger <i>et al</i> ^[7]	3	Pain (mild to moderate)
Outwater <i>et al</i> ^[10]	1	Limited ROM
Stewart ^[3,5,10]	1	Pain (intermittent)
Jones <i>et al</i> ^[6]	3	Pain
Lissens <i>et al</i> ^[8]	2	
Greenspan <i>et al</i> ^[4]	3	
Vierboom <i>et al</i> ^[13]	1	Pain (worsening)
Latifi ^[3,5-7,10]	1	
Tait ^[3,5-7,10]	1	
Berthelot <i>et al</i> ^[3]	2	
Hsu <i>et al</i> ^[5]	1	
Rand <i>et al</i> ^[14]	4	Pain (intermittent) Discomfort in the sterno-clavicular joint
Noonan <i>et al</i> ^[9]	1	Pain (chronic)
Sng <i>et al</i> ^[11]	9	Pain Discomfort in the sterno-clavicular joint
Imran ^[3,5-7,10]	1	
Present study (2016)	7 (bilateral)	Pain Discomfort in the sterno-clavicular joint
Total	58 patients (59 clavicles)	

ROM: Range of movement.

Follow-up

The mean length of follow-up was 4 years (range 2-7). At last follow-up visit none of the patients complained of pain. All reported a significant remission of pain and a marked reduction in the swelling on the medial half of the affected clavicle.

DISCUSSION

This study reviewed 7 skeletally immature patients with condensing osteitis of the clavicle. We found that an appropriate IV and oral antibiotic treatment could lead to a significant remission of signs and symptoms in children and adolescents with condensing osteitis of the clavicle (Figure 4).

Since its first description by Brower *et al*^[1] in 1974, very few cases of condensing osteitis of the clavicle have been reported in the English-language literature (Table 2).

In 1991 Greenspan *et al*^[4] highlighted the rarity of this condition and reported three new proven cases, to be added to the 13 previously reported. The first reported cases all occurred in middle-aged women. It was only in 1983 that Appell *et al*^[2] observed this clinical

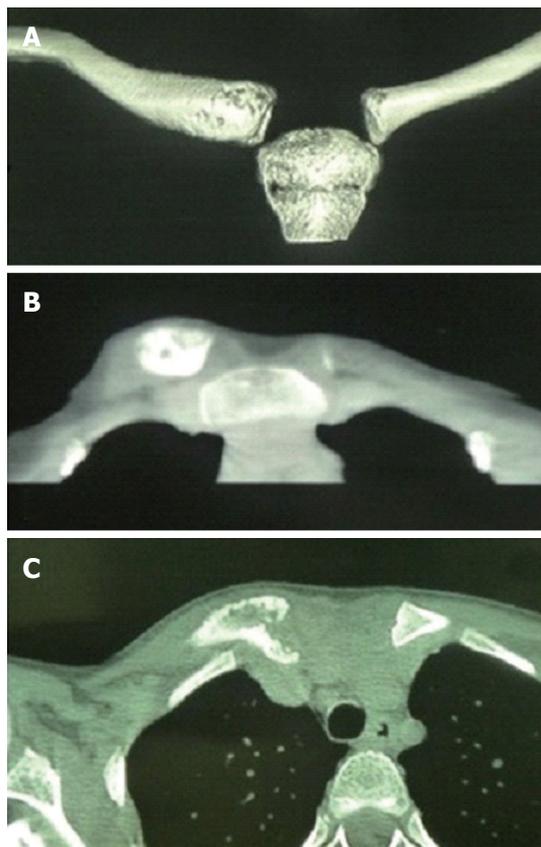


Figure 2 Computed tomography scan with three-dimensional reconstruction (A) of the right clavicle in a patient with condensing osteitis (B, C).

feature at a pediatric age. Noonan *et al*^[9] described the first male adult patient in 1998.

Although many etiopathogenetic hypotheses have been suggested for this disease, its exact cause still remains unknown. Originally, the condition was considered as a response to abnormal and repetitive mechanical stresses, such as might occur with the lifting of heavy loads. In the case of children and adolescents, this hypothesis might be linked to the carrying of a school backpack on a single brace^[2].

However, in 1987, Kruger *et al*^[7] described 3 women affected by condensing osteitis with no risk factor. One year later, Outwater and Oates^[10] reviewed 11 cases with no history of direct trauma. They suggested that osteonecrosis might play an important role in the pathogenesis of this disorder, noting that devitalized bone and marrow fibrosis with remodeling of cancellous bone may be observed in condensing osteitis.

In 1990, Jones *et al*^[6] reported three new cases of children with clinical and radiological evidence of condensing osteitis of the clavicle, and concluded that the disorder might be due to low-grade staphylococcal osteomyelitis.

In 1995, Berthelot *et al*^[3] pointed out that the disease tended to occur in bone areas overlaid by fibrocartilage, while not affecting the joint areas covered by hyaline cartilage. They therefore suggested that fibrocartilage might play an important role in the

Table 3 Differential diagnosis

Disease	Clinical and/or radiological features
Osteoarthritis	Narrowed joint space with marginal osteophytes, sclerosis restricted to the sub-chondral bone on both sides of the joint
Infection	Bone destruction, synovial abnormality, joint space narrowing, and periosteal reaction
Chronic, sclerosing osteomyelitis	Dense sclerosis similar to condensing osteitis of the clavicle, but periosteal reaction and/or foci of bone destruction
Osteoblastic lesion	Different age at onset, shorter duration of symptoms, epiphyseal location is atypical, periosteal reaction ± bony destruction, progression on serial studies
Metastases	As a solitary bone scan abnormalities in the clavicle epiphysis (unusual)
Osteoid osteoma	Classic central lucent nidus
Sternoclavicular hyperostosis	Usually bilateral, ossification of sterno-clavicular ligaments, bone scan abnormalities at sternum superior ribs, spinal ligamentous ossification and sacro-iliac abnormalities, systemic and specific dermatologic manifestations (palmoplantar pustulosis)
Friedreich's disease	Shorter duration of symptoms, clearer relationship to trauma, bone scan similar, X-rays similar ± subchondral irregularity and focal lucencies, biopsy: Osteonecrosis is typical (but marrow fibrosis or osteonecrosis have been described in several cases of condensing osteitis of the clavicle)
Tietze's syndrome	Involvement of one or more costal cartilages, the clavicle is not involved on radiographs or scan
Chronic recurrent multifocal osteomyelitis	The lesion is initially lytic and with healing, sclerotic and expansile, involves the middle two thirds sparing the medial end, and is typically at presentation. Inflammatory process can be seen at histological examination
Paget's disease	Greater area involved, and the bone scan dramatically more abnormal, localizations in other bones, elevated level of alkaline phosphatase occurs in adults

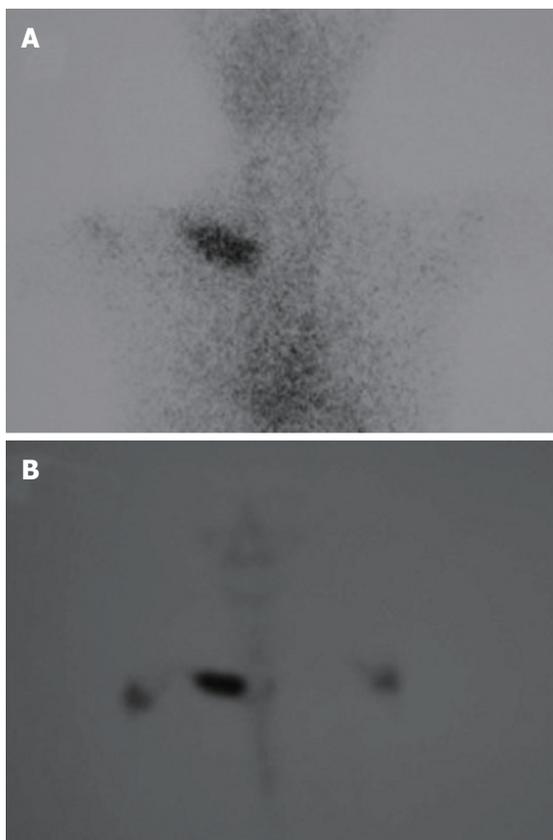


Figure 3 Triphasic bone scan showing strong, localized and isolated hyperfixation of the tracer at the level of the medial end of the right clavicle (A, B).

pathogenesis of the disease.

In 1978, Teates *et al.*^[12] pointed out the usefulness of a radionuclide bone scan in the diagnostic process; the radionuclide bone scan is characterized by a significant uptake of the tracer at the level of the affected clavicle. All our patients underwent TBS, and we found a strong,

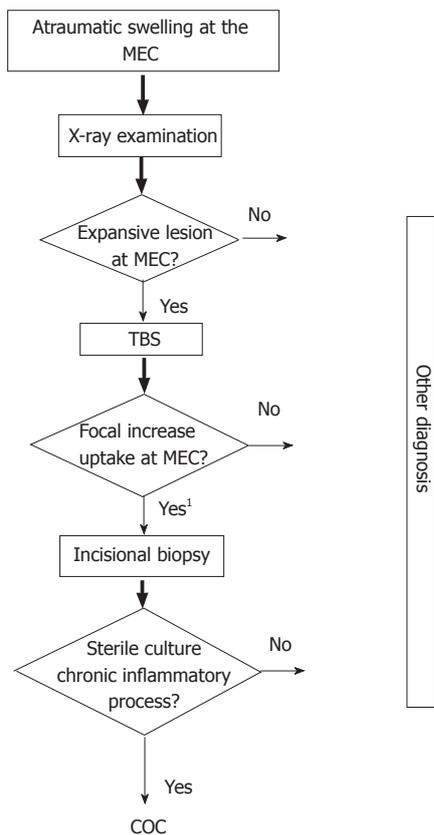


Figure 4 Diagnostic algorithm. ¹If any doubt, first perform MRI or CT scan. MRI: Magnetic resonance imaging; TBS: Triphasic bone scan; MEC: Medial end of clavicle; COC: Condensing osteitis of the clavicle.

localized and isolated hyperfixation of the tracer at the level of the medial half of the affected clavicle in all cases.

During the 1990s MRI proved a useful non-invasive procedure for the diagnosis of condensing osteitis of the clavicle. MRI can reveal edema and sclerosis of the clavicle, most probably indicative of different stages

in the disease^[13,14]. In all our patients MRI showed morphological alterations of the affected clavicle, and edema of the surrounding soft tissues in all cases.

Although Berthelot *et al*^[3] reported some cases of spontaneous remission, the condition often requires treatment. Kruger *et al*^[7] and Lissens *et al*^[8] report that non-steroidal and anti-inflammatory medications have proved effective in relieving the pain. However, resection of the medial end of the clavicle may be required in refractory cases^[4,7,8]. On the other hand, Jones *et al*^[6] observed complete remission of symptoms in the case of antibiotic therapies.

Over the years, a number of different treatment options have been described, including radiotherapy, chemotherapy, injection of corticosteroids, and surgical resection of the medial end of the clavicle in refractory cases^[4,5,7,8]. However, the best treatment option for this condition is still unknown.

In conclusion, the rarity of this pathology is highlighted by the fact that fewer than 60 proven cases have been reported in the scientific literature (Table 2). Nevertheless, the appearance of a non-traumatic swelling of the clavicle, even in the pediatric age group, should evoke this rare disorder, which should be considered in differential diagnosis (Table 3).

The potential consequences of a missed diagnosis are that the patient may undergo unnecessary, extensive and costly clinical and radiological investigations, especially if the lesion is thought to be metastatic. Furthermore, although the etiology remains unclear (seemingly either mechanical or an infectious), the complete remission of symptoms reported in our case series as a consequence of the antibiotic treatment suggests an infectious etiology, as in Jones' hypothesis^[6]. Biopsy is, however, necessary to confirm the diagnosis.

We therefore recommend approaching the disease with an appropriate IV and oral antibiotic therapy in order to avoid unnecessary aggressive surgery. Antibiotic treatment should start after the pathology report has confirmed the diagnosis. Resection of the affected medial half of the clavicle should be reserved for refractory cases only.

COMMENTS

Background

Condensing osteitis of the clavicle is a rare benign disorder of unknown origin that should be recognized promptly. It is characterized by pain and swelling at the medial end of the clavicle, with increased radio-density. Biopsy is needed to confirm diagnosis. The condition should be treated by parenteral and oral antibiotic therapy.

Research frontiers

The potential consequences of a missed diagnosis are that the patient may undergo unnecessary, extensive and costly clinical and radiological investigations, especially if the lesion is thought to be metastatic. Biopsy is necessary to confirm the diagnosis.

Innovations and breakthroughs

The disease should be approached with an appropriate intra venous (IV)

and oral antibiotic therapy in order to avoid unnecessary aggressive surgery. Antibiotic treatment should start after the pathology report has confirmed the diagnosis. Resection of the affected medial half of the clavicle should be reserved for refractory cases only.

Applications

The study results suggest that IV and oral antibiotic therapy is effective in controlling the disease.

Terminology

Condensing osteitis of the clavicle is a rare benign disorder of unknown origin that should be recognized promptly. It is characterized by pain and swelling at the medial end of the clavicle, with increased radio-density.

Peer-review

The manuscript has been described very well. Although it is a case series, the authors summarized the previous literature and presented well.

REFERENCES

- 1 **Brower AC**, Sweet DE, Keats TE. Condensing osteitis of the clavicle: a new entity. *Am J Roentgenol Radium Ther Nucl Med* 1974; **121**: 17-21 [PMID: 4833884 DOI: 10.2214/ajr.121.1.17]
- 2 **Appell RG**, Oppermann HC, Becker W, Kratzat R, Brandeis WE, Willich E. Condensing osteitis of the clavicle in childhood: a rare sclerotic bone lesion. Review of literature and report of seven patients. *Pediatr Radiol* 1983; **13**: 301-306 [PMID: 6646881 DOI: 10.1007/BF01625953]
- 3 **Berthelot JM**, Mabilie A, Nombalais MF, Maugars Y, Robert R, Prost A. Osteitis condensans of the clavicle: does fibrocartilage play a role? A report of two cases with spontaneous clinical and roentgenographic resolution. *Rev Rhum Engl Ed* 1995; **62**: 501-506 [PMID: 8574613]
- 4 **Greenspan A**, Gerscovich E, Szabo RM, Matthews JG. Condensing osteitis of the clavicle: a rare but frequently misdiagnosed condition. *AJR Am J Roentgenol* 1991; **156**: 1011-1015 [PMID: 2017922 DOI: 10.2214/ajr.156.5.2017922]
- 5 **Hsu CY**, Frassica F, McFarland EG. Condensing osteitis of the clavicle: case report and review of the literature. *Am J Orthop (Belle Mead NJ)* 1998; **27**: 445-447 [PMID: 9652888]
- 6 **Jones MW**, Carty H, Taylor JF, Ibrahim SK. Condensing osteitis of the clavicle: does it exist? *J Bone Joint Surg Br* 1990; **72**: 464-467 [PMID: 2341449]
- 7 **Kruger GD**, Rock MG, Munro TG. Condensing osteitis of the clavicle. A review of the literature and report of three cases. *J Bone Joint Surg Am* 1987; **69**: 550-557 [PMID: 3553197]
- 8 **Lissens M**, Bruyninckx F, Rosselle N. Condensing osteitis of the clavicle. Report of two cases and review of the literature. *Acta Belg Med Phys* 1990; **13**: 235-240 [PMID: 2097868]
- 9 **Noonan PT**, Stanley MD, Sartoris DJ, Resnick D. Condensing osteitis of the clavicle in a man. *Skeletal Radiol* 1998; **27**: 291-293 [PMID: 9638842 DOI: 10.1007/s002560050384]
- 10 **Outwater E**, Oates E. Condensing osteitis of the clavicle: case report and review of the literature. *J Nucl Med* 1988; **29**: 1122-1125 [PMID: 3286838]
- 11 **Sng KK**, Chan BK, Chakrabarti AJ, Bell SN, Low CO. Condensing osteitis of the medial clavicle--an intermediate-term follow-up. *Ann Acad Med Singapore* 2004; **33**: 499-502 [PMID: 15329764]
- 12 **Teates CD**, Brower AC, Williamson BR, Keats TE. Bone scans in condensing osteitis of the clavicle. *South Med J* 1978; **71**: 736-738 [PMID: 663708 DOI: 10.1097/00007611-197806000-00035]
- 13 **Vierboom MA**, Steinberg JD, Mooyaart EL, van Rijswijk MH. Condensing osteitis of the clavicle: magnetic resonance imaging as an adjunct method for differential diagnosis. *Ann Rheum Dis* 1992; **51**: 539-541 [PMID: 1586258 DOI: 10.1136/ard.51.4.539]
- 14 **Rand T**, Schweitzer M, Rafii M, Nguyen K, Garcia M, Resnick D. Condensing osteitis of the clavicle: MRI. *J Comput Assist Tomogr* 1998; **22**: 621-624 [PMID: 9676456 DOI: 10.1097/00004728-1998

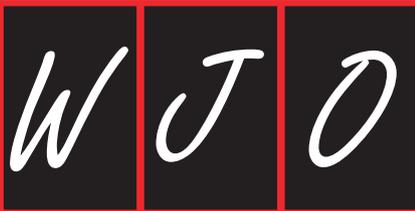
07000-00021]

15 Cochrane Handbook for Systematic Reviews of Interventions.

[accessed 2016 Jan 1]. Available from: URL: <http://www.handbook.cochrane.org>

P- Reviewer: Tawonsawatruk T, Vulcano E **S- Editor:** Gong XM
L- Editor: A **E- Editor:** Wu HL





Observational Study

Four corner fusion using a multidirectional angular stable locking plate

Tahseen Chaudhry, Michelle Spiteri, Dominic Power, Mark Brewster

Tahseen Chaudhry, Michelle Spiteri, Dominic Power, Mark Brewster, Department of Hand Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH, United Kingdom

Author contributions: Chaudhry T contributed to design and planning, protocol, data collection and processing, literature review, paper write up and revisions; Spiteri M contributed to data collection and processing, literature review; Power D contributed to study design and setup, data collection, paper review; Brewster M contributed to design and planning, protocol, data collection and processing, literature review.

Institutional review board statement: The study met the requirements of our hospital Institutional Review Board for clinical research. None of the authors have any conflict of interest to declare.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: None of the individual authors of this paper have any conflicts of interest.

Data sharing statement: No additional data are available for this study. All data are included in the paper itself.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Tahseen Chaudhry, Department of Hand Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, United Kingdom. tahseen_c@hotmail.com
Telephone: +44-1217-775956

Fax: +44-1213-712000

Received: January 31, 2016
Peer-review started: February 1, 2016
First decision: March 24, 2016
Revised: May 11, 2016
Accepted: June 1, 2016
Article in press: June 3, 2016
Published online: August 18, 2016

Abstract

AIM: To review the results of our experience with the Medartis Aptus plating system for four corner arthrodesis of the wrist, which uses a combination of compression screws and variable angle locking screws.

METHODS: We reviewed the results of 17 procedures in 16 patients that underwent scaphoid excision and four corner fusion using the Medartis Aptus system between May 2010 and June 2014. The primary outcome measure was radiographic and clinical union.

RESULTS: The mean clinical follow up time was 20.6 mo. The mean union time was 6 mo. Two non-unions required revision procedures. The mean disabilities of the arm, shoulder and hand score taken after union was 36. The mean final grip strength was 27 kg. The mean final range of movement was 30° flexion and 31° of extension. All patients had a restored scapholunate angle on postoperative radiographs. There were no incidences of dorsal impingement.

CONCLUSION: Overall our experience with the Aptus plating system shows comparable results to other methods of fixation for four corner fusion, in the short to medium term.

Key words: Wrist surgery; Arthrodesis; Locking plate;

Scaphoidectomy; Partial fusion

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This paper demonstrates that a multi angle locking plate is a suitable device for four corner fusion. It demonstrates that results are comparable to those of other means of fusion in the short to medium term.

Chaudhry T, Spiteri M, Power D, Brewster M. Four corner fusion using a multidirectional angular stable locking plate. *World J Orthop* 2016; 7(8): 501-506 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/501.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.501>

INTRODUCTION

Scaphoidectomy with four corner fusion is a well recognised surgical option for scapholunate advanced collapse (SLAC) and scaphoid non-union advanced collapse (SNAC) when the radio-lunate joint is preserved^[1]. Multiple fixation options have been employed including K wires, headless screws, staples and plates^[2-4]. Many techniques have been associated with significant complications. Circular "hub-cap" plates in particular have been associated with complications such as non-union and dorsal plate impingement^[3,5]. In response to this, newer implants are increasingly being trialled including memory staples and plates with newer designs such as the carpal fusion plate^[6,7]. Medartis™ (Basel, Switzerland) have designed the APTUS™ four corner fusion plate with some design variations compared to previous plates aimed at improving union rates and decrease dorsal impingement. Results of this plate have not previously been reported in the literature.

MATERIALS AND METHODS

A retrospective review of cases undergoing treatment with the Medartis APTUS™ Four Corner Fusion plate was performed in our unit. Cases performed at The University Hospital Birmingham and the Royal Orthopaedic Hospital were identified from a review of operating logs between May 2010 and June 2016, and the patients reviewed. Indications for surgery, associated procedures, pre-operative radiographic deformity and lunate type in particular were noted. Time to union, complications and need for further surgery were also assessed. At follow up patients also had their wrist range of movement assessed with flexion and extension measured according to the method described by Kendal *et al*^[8] with a goniometer placed dorsally over the wrist and flexion measured on the ulnar border of the wrist. Grip strength was measured using a dynamometer (Jamar dynamometer; Sammons

Preston Roylan, Bollingbrook Illinois) with the best grip strength of three trials of each surgically treated wrist compared with that of the opposite wrist (except in the one case of bilateral four corner fusion). A disabilities of the arm, shoulder and hand (DASH) score survey was also performed. All assessments were performed by four consultant hand surgeons within the 2 hospitals.

The study met the requirements of our hospital Institutional Review Board for clinical research. None of the authors have any conflict of interest to declare.

Surgical technique

All surgeries were performed by one of four hand surgeons at the Birmingham Hand Centre (which entails a group of hand surgeons working at both hospitals). All surgeons used the same dorsal approach under tourniquet control following intravenous antibiotics. A regional block was used in all cases except when iliac crest bone graft was taken. In all cases a dorsal 3-4 approach through the extensor retinaculum was used. A dorsal wrist ligament preserving approach was used, extending up along the radial styloid^[9]. The radio-lunate articular surfaces were assessed either by arthroscopy or direct vision to ensure the joint was well preserved. The scaphoid was excised and where possible used for bone graft. A radial styloidectomy was performed in 1 case. The interfacing chondral surfaces of the four bones were denuded with a nibbler, curved periosteal elevator and osteotome leaving the very volar aspects untouched to maintain the normal gap between adjacent bones. Where subchondral bone was sclerotic, further holes were created with a K wire to allow maximal bone bleeding.

K wires were inserted into the carpal bones to realign the capitate and lunate and if necessary stabilise the hamate and triquetrum (only required about half the time). This was performed in 2 main ways: (1) an antegrade 1.6 mm K wire from radius to lunate (once the radiolunate angle had been corrected by flexion or extension of the wrist) and then advanced onto the capitate once a neutral capito-lunate angle was achieved and the radio-ulna translation corrected (often the capitate tries to slip off the lunate radially); and (2) a retrograde wire is passed between the second and third metacarpal bases with around 20 degrees of elevation off the hand, through the capitate and onto the lunate, which allows correction of any carpal malalignment present. Both K wire insertion methods are technically difficult due to the angles required and in addition the wire needs to be seated palmar in both bones to allow for the subsequent reamer to cut freely.

During K wire introduction it is important to reduce the capitate into the lunate, which can be especially difficult in type 2 lunates in which there is a tendency for the capitate to slip off the lunate radially.

A custom APTUS™ reamer is then placed in the cross of the 4 bones to allow the plate to be countersunk. It is important to ream the bones to equal depths especially

Table 1 Patient and surgery characteristics, time to union and follow up

Number	Age	Sex	Hand	Classification	Lunate type	VISI/DISI	Associated surgery	No. of screws	Union (mo)	Complications	Follow up (mo)
1a	64	M	L	SLAC	1		PIN	11	4		30
1b	65	M	R	SLAC	1		PIN	11	6		24
2	52	F	R	SLAC	2	V	PIN	12	3		10
3	40	M	L	SLAC	1	D	Distal radius graft (previous PIN)	12	9		11
4	38	M	L	SNAC	1	D	PIN + styloidectomy	11	16	Screws Penetrating CMC joint	35
5	72	F	L	SNAC	1	D	PIN + Iliac BG	8	3		8
6	55	M	L	SNAC	2	D	PIN + distal radius graft	11	2		18
7	61	M	R	SNAC	2	D	PIN + distal radius graft	11	3		10
8	33	M	L	Lunate fracture	1	V	PIN	12	17 ¹	Non-union, revised	23
9	35	M	L	SNAC	2		PIN	11	7	Hypertrophic bone	16
10	50	M	R	SNAC	2		PIN	10	6	Scar sensitivity	25
11	55	M	L	SNAC	1		PIN	10	4		26
12	46	M	L	SNAC	2	D	PIN	12	7		25
13	48	F	L	SNAC	1	D	PIN	12	5		25
14	40	M	R	SNAC	2		PIN	12	8	Skin necrosis over plate + flap coverage	24
15	18	M	R	Scaphoid	2		PIN, plate removal distal radius graft	10	9		16
16	50	M	R	SLAC	1		PIN	12	27 ¹	Non-union, revised	27

¹Indicates total time to final union including both index procedure and revision surgery. PIN: Posterior interosseous neurectomy; M: Male; F: Female; L: Left; R: Right; SLAC: Scapholunate advanced collapse; SNAC: Scaphoid nonunion advanced collapse; V: VISI; D: DISI; BG: Bone graft; CMC: Carpometacarpal.

on the lunate to allow the plate to be flush of deep to the dorsal lip to avoid dorsal impingement on wrist extension.

In some cases additional dorsal radial or iliac crest graft was taken to pack between the bones and this can be further compressed by reaming on a reverse setting with the bone graft *in situ*.

Once the plate is seated, inner non-locking compression screws are inserted to secure the four bones. Outer multidirectional (30 degree arc of variability) locking screws were then inserted. However if an angle outside the 30 degree arc is required to gain carpal purchase, a non locking screw can be used in these outer holes. The triquetrum was included in all fusions. An image intensifier was used throughout to check implant and carpal positions.

There was a variation in post-operative immobilisation from wool and crepe to 6 wk in a below elbow plaster (Table 1). If a cast was used for less than 6 wk patients began active mobilisation with a removable thermoplastic splint for comfort. From six weeks post-operative date onwards signs of union were assessed at regular intervals clinically by a lack of tenderness at the fusion site and/or with radiographic evidence of bridging trabeculae between the bones (although this was appreciably difficult due to the multiple overlapping cortices seen on plain radiographs (Figure 1A). Dorsal impingement was identified according to the description of Shindle *et al*^[3] by the patient complaining of a sharp dorsal pain with maximal passive or active wrist extension.

RESULTS

Seventeen procedures were performed on sixteen patients, 13 men and 3 women. The demographic data of the patients is included in Table 1. The mean age of the patients was 48 years (range 18-72 years). Ten operations were on a left wrist, seven on a right wrist. The indications were SLAC grade 2 in three wrists, grade 3 in two wrists and SNAC in ten wrists. One case was a salvage procedure for a failed fixation of a scaphoid fracture, another was a salvage procedure for a lunate fracture. Typical pre-operative appearances are shown in Figure 1.

The mean follow up time was 20.6 mo (range 8-35). Excluding the two non-unions that required revision procedures, the mean time to union on radiographic and clinical assessment was 6 mo (range 3-16). All fusions ultimately united including the two that required revision surgery. One case united after 16 mo but multiple screws were found to have broken during the follow up period. This patient went on to undergo metalwork removal as one screw penetrated the fifth carpometacarpal joint.

The final range of movement was invariably reduced compared to the contralateral side. The mean final flexion was 30 degrees (20-45) and the mean final extension was 31 degrees (10-60). There were no instances of dorsal impingement from the plate. Post-operative radiographs for a number of patients were taken in full wrist extension, and these demonstrated the ability of the plate to remain deep to the dorsal lip

Table 2 Outcomes at discharge or at latest follow up

Number	JAMAR (kg) (unaffected)	% grip strength difference	Flexion (unaffected)	Extension (unaffected)	DASH	Return to work	Satisfied?
1a	22	NA	30	20	43	Retired	Yes
1b	24	NA	25	40	43	Retired	Yes
2	11 (26)	42%	25 (50)	15 (40)	48	Office	Yes
3	30 (36)	83%	45	45	15	Office	Yes
4	32 (37)	87%	35 (92)	18 (80)	48	Heavy manual	Yes
5	4 (18)	22%	30	10	35	Retired	Yes
6	48 (32)	150%	30	45	20	Office	Yes
7	25 (38)	66%	45	45	13	Retired	Yes
8	22 (55)	40%	30	20	61	No	No
9	36 (48)	75%	20	10	43	No	Yes
10	30 (40)	75%	30	60	20	Office	Yes
11	18 (52)	35%	20	20	35	Office	Yes
12	26 (35)	74%	40	40	15	Yes	Yes
13	25 (30)	83%	20	50	13	Manual	Yes
14	45 (35)	129%	30	40	42	No	No
15	20 (38)	53%	20	35	15	Office	Yes
16	40 (55)	73%	30	15	27	Office	Yes

Data for the unaffected wrist where available are given in brackets. DASH: Disabilities of the arm, shoulder and hand.

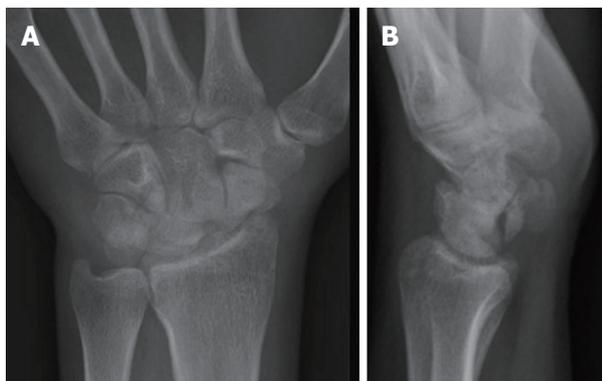


Figure 1 A posterior-anterior (A) and lateral (B) view of a typical Scapholunate advanced collapse wrist prior to undergoing four corner fusion.

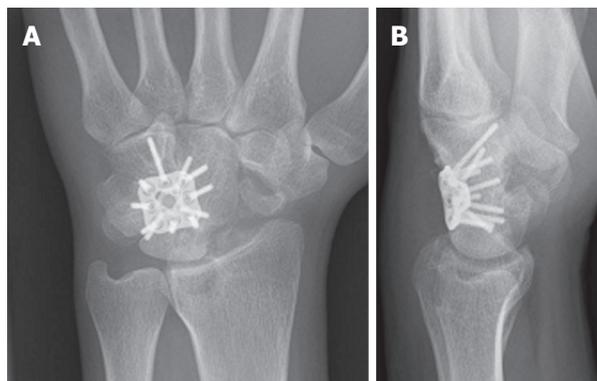


Figure 2 A postero-anterior (A) and lateral (B) view of the plate in its final position.

of the radius in extension (Figure 1A).

All patients had a restored scapholunate angle on postoperative radiographs (Mean = 60°). The mean capitulate angle was 3° (range: 15°-3°)

Typical post-operative X-ray and computed tomography appearances are shown in Figures 2 and 3.

The mean final grip strength was 27 kg (range: 4-48) which represented 72% (22%-129%) of the unaffected side. The mean DASH score at the latest follow up was 32 (13-61).

Table 2 shows that all but two patients managed to return to their previous occupation.

Two patients remain unsatisfied at the last follow up for reasons mentioned below. One is awaiting a wrist arthroscopy and the other had skin necrosis around the dorsal wound requiring flap coverage. No additional data are available.

Complications

One patient had broken screws that were impinging on

the 5th CMCJ and required removal.

One patient had a very sensitive scar that failed to settle down during the follow up period.

Two patients exhibited radial drift, with the trapezium abutting the radius on post operative radiographs. Neither had any associated clinical symptoms. A further patient had an area of skin necrosis over the dorsal wrist incision site and required debridement and a radial forearm flap to cover the soft tissue defect. He has made a good functional recovery but is significantly affected by the cosmetic appearance of his wrist.

Two patients failed to unite by 15 mo and were therefore revised with the same implant. Both went onto unite successfully. One of these patients has returned to work and is satisfied, and the other has ongoing ulnar sided wrist pain which is awaiting a wrist arthroscopy.

DISCUSSION

In the setting of SNAC and SLAC wrists, scaphoidectomy and four corner fusions with a plate is very attractive.

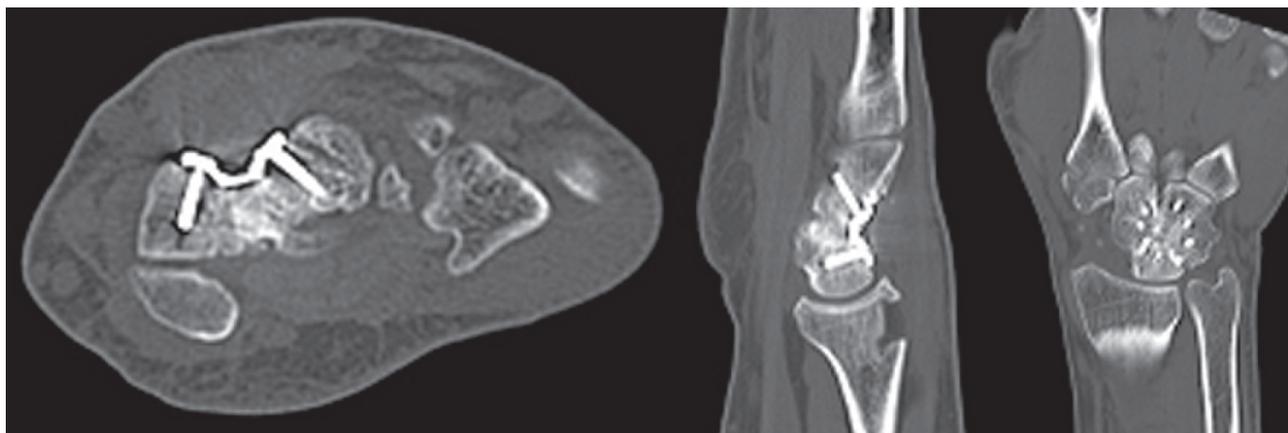


Figure 3 Coronal, Sagittal and axial, postoperative views following plate application and fusion.

Compared to fixation techniques such as K wires, four corner fixation plates have the potential advantages of increased stability, higher fusion rates, shorter periods of immobilisation and improved range of motion^[8].

The design of the Medartis APTUS™ plate arose from documented concerns with previous circular dorsal plates^[3,5]. Complications included radiographic non-union rates as high as 62.5% dorsal impingements as frequent as 25% and an overall complication rate of up to 56%^[3,8]. The Medartis™ plate design is low profile (1.4 mm thick) and has variable screw fixation options. The carpus is reamed to allow the plate to sit sunken within the carpal bones, to minimise plate impingement on the dorsal lip of the radius. There was no evidence of dorsal impingement in our study.

The Medartis™ plate (which comes in 2 sizes, 17 and 15 mm diameter) allows compression with central non-locking screws as well as locking screw fixation. Each locking screw can be inserted within a 30 degree arc (locked with a unique Trilock™ system allowing adjustment of the screw angle up to 3 times), this allows for greater adjustment by the surgeon to get optimal bony purchase with the screws. Locking screws are theoretically stronger than traditional screws as was borne out in Kraissarin's cadaveric study^[10]. Locking screws alone may hinder compression at the fusion site and fix the carpus bone in a distracted position^[8]. They may also create too rigid a construct to allow interfragmentary motion, a factor which we think occurred in our case when several screws broke. The high fusion rate of implants that allow compression including K wires memory staples and the carpal fusion system plate highlights the need for compression in a four corner fusion^[6,7,11].

Hence, by allowing compression prior to locking fixation, the Medartis™ plate appears to promote fusion over previous dorsal plate designs.

All patients in our study reported mild to no pain following surgery, in contrast to Kendall *et al*^[8] but in keeping with other studies^[12]. In all cases a PIN neurectomy was performed at the time of surgery, except in

one case when the PIN neurectomy had previously been performed. Pain tended to be located over the ulnar side of the wrist in flexion and ulnar deviation.

The patients in our study fixed with the Medartis APTUS™ plate appeared to have a relatively long time to fusion. It is known however that time to union is difficult to diagnose on plain radiographs as the circular plate blocks the area of fusion and hence some authors only diagnose a non-union where a secondary procedure is required^[3,8]. Whilst we used clinical assessment to diagnose carpal fusion, this has not been validated. As time to union may not be an objective measurement, it may be that the need for a secondary procedure for fusion as reported by Kendall *et al*^[8] is more useful.

Our mean follow up is just under two years. A long term follow up study of four corner fusions suggests that most complications occur with a two year initial period after which there is long term satisfaction with the procedure^[13].

The main limitation with this study, in that, it involved a relatively small retrospective cohort. Furthermore, the addition of pre-operative range of motion, grip strength and DASH scores would have been a useful adjunct to this data. We believe that our data support performing a PIN neurectomy at the time of surgery as well as using an inset circular plate that allows both compression and locking screw fixation of the carpus. With an improvement of wrist plates specifically designed for four corner fusion, there will hopefully be an improvement in the results of four corner fusion to match the high success and low complication rates of total wrist fusion.

COMMENTS

Background

Scaphoidectomy with four corner fusion is a well recognised surgical option for scapholunate advanced collapse (SLAC). A variety of fixation methods have been tried and the newest implants are plates of various designs.

Research frontiers

Many of the current plates have problems with non-union or impingement.

Innovations and breakthroughs

The Medartis Aptus plate has some design variations compared to previous plates aimed at improving union rates and decrease dorsal impingement. These may be achieved through its multiangle locking configuration as well as its cortical screw holes and low profile design.

Applications

This plate is a useful solution for four corner arthrodesis in patients with SLAC or scaphoid non-union advanced collapse.

Terminology

SLAC wrist: Scapholunate advanced collapse.

Peer-review

It is a well written manuscript overall that worth publishing.

REFERENCES

- 1 **Watson HK**, Ballet FL. The SLAC wrist: scapholunate advanced collapse pattern of degenerative arthritis. *J Hand Surg Am* 1984; **9**: 358-365 [PMID: 6725894 DOI: 10.1016/S0363-5023(84)80223-3]
- 2 **Vance MC**, Hernandez JD, Didonna ML, Stern PJ. Complications and outcome of four-corner arthrodesis: circular plate fixation versus traditional techniques. *J Hand Surg Am* 2005; **30**: 1122-1127 [PMID: 16344166 DOI: 10.1016/j.jhsa.2005.08.007]
- 3 **Shindle MK**, Burton KJ, Weiland AJ, Domb BG, Wolfe SW. Complications of circular plate fixation for four-corner arthrodesis. *J Hand Surg Eur Vol* 2007; **32**: 50-53 [PMID: 17049699 DOI: 10.1016/j.jhsb.2006.08.016]
- 4 **Ball B**, Bergman JW. Scaphoid excision and 4-corner fusion using retrograde headless compression screws. *Tech Hand Up Extrem Surg* 2012; **16**: 204-209 [PMID: 23160552 DOI: 10.1097/BTH.0b013e3182688c6a]
- 5 **Stanley JK**. Re: Mulford JS, Ceulemans LJ, Nam D, Axelrod TS. Proximal row carpectomy vs. four corner fusion for scapholunate (SLAC) or scaphoid nonunion advanced collapse (SNAC) wrists: a systematic review of outcomes. *J Hand Surg Eur*. 2009, **34**: 256-63. *J Hand Surg Eur Vol* 2009; **34**: 819-820; **author reply 820** [PMID: 20067934 DOI: 10.1177/1753193408100954]
- 6 **Van Amerongen EA**, Schuurman AH. Four-corner arthrodesis using the Quad memory staple. *J Hand Surg Eur Vol* 2009; **34**: 252-255 [PMID: 19129362 DOI: 10.1177/1753193408094444]
- 7 **Allison DM**. A new plate for partial wrist fusions: results in midcarpal arthrodesis. *J Hand Surg Eur Vol* 2011; **36**: 315-319 [PMID: 21282216 DOI: 10.1177/1753193410395357]
- 8 **Kendall CB**, Brown TR, Millon SJ, Rudisill LE, Sanders JL, Tanner SL. Results of four-corner arthrodesis using dorsal circular plate fixation. *J Hand Surg Am* 2005; **30**: 903-907 [PMID: 16182043 DOI: 10.1016/j.jhsa.2005.04.007]
- 9 **Berger RA**. A method of defining palpable landmarks for the ligament-splitting dorsal wrist capsulotomy. *J Hand Surg Am* 2007; **32**: 1291-1295 [PMID: 17923317 DOI: 10.1016/j.jhsa.2007.07.023]
- 10 **Kraisarin J**, Dennison DG, Berglund LJ, An KN, Shin AY. Biomechanical comparison of three fixation techniques used for four-corner arthrodesis. *J Hand Surg Eur Vol* 2011; **36**: 560-567 [PMID: 21636620 DOI: 10.1177/1753193411406799]
- 11 **Ashmead D**, Watson HK, Damon C, Herber S, Paly W. Scapholunate advanced collapse wrist salvage. *J Hand Surg Am* 1994; **19**: 741-750 [PMID: 7806794 DOI: 10.1016/0363-5023(94)90177-5]
- 12 **Wyrick JD**, Stern PJ, Kiefhaber TR. Motion-preserving procedures in the treatment of scapholunate advanced collapse wrist: proximal row carpectomy versus four-corner arthrodesis. *J Hand Surg Am* 1995; **20**: 965-970 [PMID: 8583069 DOI: 10.1016/S0363-5023(05)80144-3]
- 13 **Trail IA**, Murali R, Stanley JK, Hayton MJ, Talwalkar S, Sreekumar R, Birch A. The long-term outcome of four-corner fusion. *J Wrist Surg* 2015; **4**: 128-133 [PMID: 25945298 DOI: 10.1055/s-0035-1549277]

P- Reviewer: Drampalos E, Vulcano E S- Editor: Ji FF
L- Editor: A E- Editor: Wu HL



Observational Study

Validation of the functional rating index for the assessment of athletes with neck pain

Soofia Naghdi, Nouredin Nakhostin Ansari, Somaye ShamsSalehi, Ronald J Feise, Ebrahim Entezary

Soofia Naghdi, Nouredin Nakhostin Ansari, Somaye ShamsSalehi, Ebrahim Entezary, Department of Physiotherapy, School of Rehabilitation, Tehran University of Medical Sciences, Tehran 11489, Iran

Ronald J Feise, Institute of Evidence-Based Chiropractic, Scottsdale, AZ 85251, United States

Author contributions: Naghdi S, Nakhostin Ansari N, and Feise RJ conceived and designed the study; ShamsSalehi S drafted the research protocol, which was edited and revised by Naghdi S, Nakhostin Ansari N, and Entezary E; ShamsSalehi S collected the data; Nakhostin Ansari N performed all the statistical analyses; Naghdi S, Nakhostin Ansari N and ShamsSalehi S drafted the manuscript, which was further edited and approved by all authors to be published; Nakhostin Ansari N was the chief investigator and guarantor.

Institutional review board statement: The study was reviewed and approved by the review board, School of Rehabilitation, Tehran University of Medical Sciences.

Informed consent statement: All subjects gave their informed consent prior to the study enrolment.

Conflict-of-interest statement: The authors have no competing interests to declare.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Nouredin Nakhostin Ansari, Professor, Department of Physiotherapy, School of Rehabilitation, Tehran

University of Medical sciences, Enghelab Ave, Pitch-e-shemiran, Tehran 11489, Iran. nakhostin@sina.tums.ac.ir
Telephone: +98-21-77533939
Fax: +98-21-77727009

Received: February 16, 2016
Peer-review started: February 18, 2016
First decision: March 25, 2016
Revised: May 8, 2016
Accepted: June 1, 2016
Article in press: June 3, 2016
Published online: August 18, 2016

Abstract

AIM: To validate the culturally-adapted Persian Functional Rating Index (PFRI) for assessing neck pain (NP) in athletes.

METHODS: In this cross-sectional study, 100 athletes with NP and 50 healthy athletes participated and responded to the PFRI. Fifty athletes with NP completed the PFRI for at least 7 d later to establish test-retest reliability.

RESULTS: The athletes with NP responded to all items, indicating excellent clinical utility. No floor and ceiling effects were found, indicating content validity and responsiveness. The PFRI revealed capability to discriminate between the athletes with NP and healthy athletes. The PFRI demonstrated strong correlation with the Numerical Rating Scale (Spearman's $\rho = 0.94$), and the Persian Neck Disability Index (Pearson $r = 0.995$), supporting criterion and construct validity. Internal consistency reliability was high (Cronbach's α coefficient: 0.97). The test-retest reliability was excellent (ICC_{agreement} = 0.96). The absolute reliability values of standard error of measurement and smallest detectable change were 3.2 and 8.84, respectively. An exploratory

factor analysis yielded one factor explaining 78.03% of the total variance.

CONCLUSION: The PFRI is a valid and reliable measure of functional status in athletes with NP.

Key words: Athletes; Neck pain; Functional rating index; Reliability; Validity

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Patient-reported outcomes are widely used to evaluate the functional effectiveness of treatments in clinical investigations. There has been a lack of patient-reported outcome measure for athletes with neck pain (NP). This study assessed the psychometric properties of the culturally-adapted Persian Functional Rating Index in a group of athletes with NP and demonstrated excellent validity and reliability.

Naghdi S, Nakhostin Ansari N, ShamsSalehi S, Feise RJ, Entezary E. Validation of the functional rating index for the assessment of athletes with neck pain. *World J Orthop* 2016; 7(8): 507-512 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/507.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.507>

INTRODUCTION

Neck pain (NP) is a common musculoskeletal complaint in athletes. The lifetime incidence of NP has been estimated at 47.6%, with approximately 64% being sports related^[1]. An epidemiological study found a relatively higher rate of NP in cycling athletes^[2]. The NP in athletes may result from sprains, strains, and soft tissue contusions resulting in various problems such as deficits in mobility, strength, endurance, and postural stability^[3-6]. In order to help the athletes with NP return quickly to their sporting function, it is important to accurately assess their symptoms and function using valid and reliable tools.

There are several disease-specific questionnaires developed to assess the functional limitations in people with spinal disorders including neck pain (*e.g.*, neck disability index, neck pain and disability scale). Any outcome tool should be validated among different populations before using in the clinical assessments. The validity of the questionnaires to measure neck related pain and disability is not established among athletes with NP. Currently, there is no validated test developed specifically for assessing NP in athletes.

The Functional Rating Index (FRI) is a patient-reported questionnaire developed to evaluate the patients' perspectives on their pain and functional status in patients with low back pain (LBP) as well as NP^[7]. The Persian FRI (PFRI) is validated in the general population with LBP^[8] and NP^[9], and it was recently validated

for athletes with LBP^[10]. The present study aims to validate the PFRI in athletes with NP. The psychometric properties of floor or ceiling effects, discriminant validity, concurrent criterion validity, construct validity, internal consistency reliability, test-retest reliability, standard error of measurement (SEM), smallest detectable change (SDC), and factor structure were evaluated.

MATERIALS AND METHODS

The protocol of this cross-sectional study was approved by the review board, School of Rehabilitation, Tehran University of Medical Sciences (TUMS). The study was performed after approval by the TUMS Ethics Committee, and all subjects gave their written informed consent for taking part in the study.

Participants

Adult athletes age ≥ 18 years with NP, participating in sport activities for at least 2 h, 3 d/wk, and be able to read and write Persian were recruited from Tehran, Iran sport clubs and included in the study. Athletes were excluded if they had osteoporosis, spinal fracture, previous spinal surgery, or rheumatologic diseases. The sample size for this study was based on the recommendation provided in the guideline; thus, 100 athletes with NP were included in the study^[11].

Procedure

We followed the procedure used for validation of the FRI in athletes with LBP^[10]. Eligible athletes were sampled from the Tehran sport clubs, Iran. The study aim and procedure were first thoroughly described to each eligible athlete. Then, after an informed consent form was read and signed by each athlete, demographic data including age, education, NP duration, and sports activities were recorded. Each eligible athlete was asked to fill out the PFRI, validated Persian Neck Disability Index (NDI)^[12], and the Numerical Rating Scale (NRS)^[13]. Fifty athletes with NP refilled out the PFRI at least 7 d later to evaluate the test-retest reliability. Fifty healthy athletes with no neck pain filled out the PFRI to assess discriminant validity. The NDI and the NRS were filled out to assess respect construct validity and concurrent criterion validity. High correlation was expected between the PFRI and NDI for construct validity.

Instruments

FRI: The FRI is a reliable and valid instrument that contains 10 items measuring both pain and function from 0 (no pain/full function) to 4 (worst possible pain/unable to perform function). The formula (total score/40) \times 100% was used to calculate the disability score ranging from 0% (no disability) to 100% (severe disability)^[7,14]. The culturally adapted and validated Persian FRI was used in this study^[8-10].

NDI: The instrument used to evaluate the construct validity was the reliable and valid NDI^[15]. The NDI

contains 10 items with each item rated from 0 (no activity limitation) to 5 (major activity limitation). The NDI total score is calculated as a percentage, with higher scores meaning greater disability. In this study, the culturally adapted Persian NDI was used^[12].

NRS: The NRS was used to assess concurrent criterion validity. With the NRS, the athletes with NP were asked to score their pain intensity between 0 (no pain) and 10 (worst possible pain)^[13,16].

Statistical analysis

The floor and ceiling effects were analyzed by calculation of percentage of the lowest (0%) and the highest (100%) scores for the total PFRI. Discriminant validity was assessed by comparing the PFRI total scores of the athletes with NP with scores of the healthy athletes using the independent *t* test. The construct validity was analyzed by examining the correlation between the PFRI and the NDI using Pearson correlation test with levels of $0.6 \geq [7]$. The Spearman rank order correlation was used to assess concurrent criterion validity by correlating the PFRI total scores to the NRS with at least 0.7 as acceptable. The Cronbach's α was applied to analyze the internal consistency reliability with a level of 0.7 or higher as satisfactory^[11]. The intraclass correlation coefficient agreement (ICC_{agreement}) (two-way random effects model, absolute agreement, and single measure) was used for the test-retest reliability analysis with a level of at least 0.70 as acceptable. The absolute reliability measures of the standard SEM and the SDC were estimated using the formulas $\sigma\sqrt{1-ICC}$ and $1.96 \times SEM \times \sqrt{2}$, respectively. A principal component analysis (PCA) with varimax rotation (VR) was used to analyze the factor structure of the PFRI. The SPSS software, V17 (SPSS, Inc, Chicago, IL) was used for the statistical analyses.

RESULTS

Overall, this study recruited 150 athletes. One hundred athletes with NP (60 male/40 female; mean age \pm SD 30.8 ± 6.7 years; education 15.0 ± 2.2 years; NP duration 3.72 ± 1.74 mo) and 50 healthy athletes (27 male/23 female; mean age 31.5 ± 7.4 years; education 15.0 ± 2.4 years) participated in the study. Of the 100 recruited athletes with NP, 50 athletes completed the PFRI again after at least 7 d (range: 7.0-32.0 d) to establish test-retest reliability.

The sports activities of athletes in this sample of athletes ($n = 150$) included bodybuilding ($n = 46$, 30.7%), aerobics ($n = 27$, 18.0%), swimming ($n = 16$, 10.7%), karate ($n = 17$, 11.3%), taekwondo ($n = 13$, 8.7%), volleyball ($n = 10$, 6.7%), soccer ($n = 9$, 6.0%), yoga ($n = 6$, 4.0%), and badminton ($n = 6$, 4.0%).

Floor and ceiling effects

The athletes with NP responded to all items, and no missing data were detected. No floor or ceiling effect

Table 1 Summary of clinical data in athletes with neck pain ($n = 100$)

Outcome measures	Mean	SD	Range	
			Minimum	Maximum
PFRI	30.85	15.94	10.00	92.500
PNDI	30.22	15.93	8.00	88.00
NRS		Median (IQR) 2 (2-3)		

PFRI: Persian functional rating index; PNDI: Persian neck disability index; NRS: Numerical rating scale; IQR: Interquartile range.

was observed for PFRI scores (range: 10.00-92.50). No athletes with NP scored the highest or lowest possible score on the PFRI. Table 1 shows the clinical data for the athletes with NP.

Validity

For discriminant validity, the PFRI scores from the 50 athletes with NP who participated in the test-retest reliability evaluation were compared with those of the healthy athletes. The PFRI scores for athletes with NP (32.2 ± 19.04) were statistically worse than those of healthy athletes (3.7 ± 2.5) (Levenes's test: $F = 69.001$, $P < 0.001$; $t = 10.5$, $df = 50.7$, $P < 0.001$).

For the evaluation of the concurrent criterion validity, Spearman's rho displayed an excellent correlation between the PFRI scores and the NRS (correlation coefficient = 0.94, $P < 0.001$; 95%CI: 0.9-0.97).

An excellent correlation was found between the PFRI and the NDI (Pearson correlation coefficient = 0.995, $P < 0.001$; 95%CI: 0.99-1.0) for construct validity.

Relative reliability

Cronbach's α coefficient of internal consistency was 0.96, and values of Cronbach's α if an item was deleted ranged between 0.961 and 0.964. Corrected item-total correlation ranged from 0.812 to 0.896 (Table 2).

ICC_{agreement} was excellent for test-retest measurements (ICC_{agreement} = 0.96, 95%CI: 0.93-0.98, $P < 0.001$) (Table 3).

Absolute reliability

The SEM and the SDC were calculated to be 3.2 (95%CI: -6.25-6.25) and 8.84, respectively (Table 3).

Factor analysis

The Kaiser-Meyer-Olkin was 0.94, which indicates the adequacy of the sample for performing the factor analysis. The Bartlett's test of sphericity produced a high χ^2 of 1107.421, $df = 45$, $P < 0.001$, which indicates that the factor model was appropriate. The PCA with VR revealed a model with 1 factor, explaining 78.03% of the total variance. Figure 1 shows the scree plot curve for factor analysis of the 10-item PFRI.

DISCUSSION

In this study, the PFRI was evaluated for validity and reliability in Persian-speaking adult athletes with NP, and

Table 2 Cronbach's alpha and item-total statistics for persian functional rating index

FRI items	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Squared multiple correlation	Cronbach's alpha if item deleted
Pain intensity	10.89	34.240	0.877	0.801	0.963
Sleeping	11.45	33.563	0.823	0.724	0.964
Personal care	11.02	33.353	0.852	0.780	0.963
Travel	10.83	31.819	0.852	0.753	0.963
Work	11.04	34.463	0.867	0.804	0.963
Recreation	11.07	33.399	0.846	0.735	0.963
Frequency of pain	10.57	32.591	0.812	0.750	0.964
Lifting	10.97	33.686	0.831	0.723	0.963
Walking	11.58	31.620	0.896	0.865	0.961
Standing	11.64	31.930	0.883	0.854	0.962

FRI: Functional rating index.

Table 3 Results of relative and absolute reliability measures for the Persian Functional Rating Index in athletes with neck pain (n = 50)

Scale	Mean ± SD		d (SD)	ICC _{agreement} (95%CI)	SEM	SDC
	Test	Retest				
PFRI	32.15 ± 19.04	30.70 ± 15.90	1.45 (4.95)	0.96 (0.93-0.98)	3.2	8.84

d: Mean difference of the test and retest scores; ICC: Intraclass correlation coefficient; SEM: Standard error of measurement; SDC: Smallest detectable change; PFRI: Persian Functional Rating Index.

it was shown to have excellent psychometric properties. All athletes with NP completed the PFRI without any problem, indicating the cultural acceptability and clinical utility of the questionnaire. The PFRI, consistent with the previous validation study in athletes with low back pain^[10], is a valid and reliable tool for measuring pain and functional status in athletes with NP. To the best of our knowledge, this is the first study validating a self-administered instrument for assessing athletes with NP.

All athletes completed the PFRI without any difficulties and with no missing responses. Responding to all questions on PFRI indicates acceptability and clinical utility. The distribution of the PFRI was satisfactory as demonstrated by the absence of floor or ceiling effects. The lack of floor or ceiling effects indicates the content validity and the responsiveness of the PFRI, in accordance with findings in athletes with LBP^[10].

When PFRI scores for athletes with NP were compared to the scores of healthy participants, the athletes with NP had significantly worse scores and function. This finding suggests that the PFRI discriminated athletes with NP from healthy controls. In a study which tested the ability of the PFRI to discriminate athletes with LBP from healthy athletes, a similar finding was found^[10]. These data indicate that the discriminant validity of the Persian FRI in athletes with NP or LBP is consistent with those observed in the general population^[8,9].

The excellent correlation between the PFRI and the NRS suggests the concurrent validity of the PFRI in

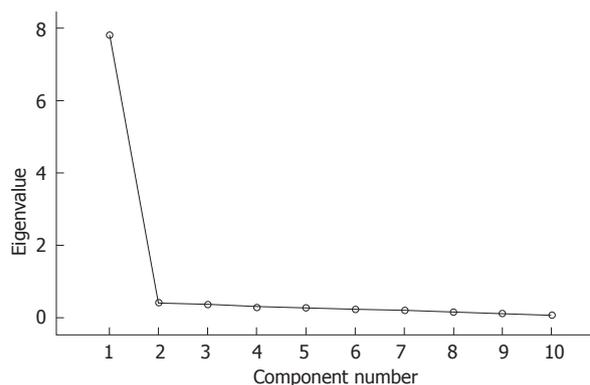


Figure 1 Scree plot of eigenvalues produced 1 factor for persian functional rating index in athletes with neck pain (n = 100).

athletes with NP. Our finding is in accordance with that in athletes with LBP ($\rho = 0.72$)^[10].

Construct validity was assessed by correlating the PFRI with the NDI, and, as hypothesized, excellent association was observed between the two tools. The significant correlation between the PFRI with the Persian NDI suggests that these two questionnaires measure similar construct. A similar result was found for the PFRI in athletes with LBP ($r = 0.83$)^[10].

The PFRI showed excellent internal consistency as reflected in a Cronbach's α value well above the minimum recommended value. Cronbach's alpha when an item was deleted was very close to the overall alpha, which indicates similar contribution of each PFRI item to the construct measured. These results support the homogeneity and interrelatedness of the PFRI items. The internal consistency found in the present study was similar to that observed by Naghdi *et al*^[10] when the PFRI was applied in athletes with LBP (Cronbach's $\alpha = 0.90$).

The test-retest reliability of the PFRI in athletes with NP between two assessment sessions was found to be excellent (ICC_{agreement} = 0.96) in agreement with the result (ICC_{agreement} = 0.97), as similarly reported in athletes with LBP^[10]. The high value of ICC_{agreement} found in this study indicated excellent reproducibility of the PFRI and consistency of the scores between two measurements.

The SEM found in this study was small, which indicates the reliability of the PFRI to identify real changes. The SDC is a useful estimate to identify real change score in an individual patient after an intervention. The SDC in the present study was 8.84%, which is clinically acceptable. This indicates only a change score greater than 9.0% can be interpreted as a real change with a 95% confidence using the PFRI. Estimation of SEM and SDC were not reported for the PFRI in athletes with LBP^[10].

Factor analysis was applied to determine the possible subscales of the PFRI despite acceptable Cronbach's α and item-total correlation values found in this study. The factor analysis resulted in a 1-factor solution for the PFRI, in accordance with results demonstrated in

athletes with LBP^[10]. The factor analysis confirmed that the PFRI assessed predominantly a distinct factor of the underlying construct concerning pain and function. This finding provides further evidence for construct validity of the PFRI. The PFRI can be used independently to identify changes in pain and function of athletes with NP.

There were limitations for the present study. First, the effect size based responsiveness of the PFRI to detect change over time was not evaluated in this study. The evaluation of floor and ceiling effects is one of the methods used for quantifying responsiveness^[17,18]. The lack of floor and ceiling effects found in this study implies that the PFRI is able to detect changes following treatment. Second, this study assessed only the Persian FRI. An English FRI must be separately validated for athletes with NP.

In conclusion, the PFRI demonstrated excellent validity and reliability, and therefore, can be used in both clinical and research settings for athletes with NP.

ACKNOWLEDGMENTS

The authors would like to thank the Research Deputy at Tehran University of Medical Sciences. We also thank the athletes who participated in the study.

COMMENTS

Background

Neck pain (NP) is one of the common complaints in athletes. Reliable and valid tests are required to accurately examine the athletes with NP. There are various self-report questionnaires [e.g., Functional Rating Index (FRI)] developed for evaluation of disability in patients with various spinal conditions such as NP. The self-report questionnaires allow the clinicians to evaluate the extent to which spinal disorders affect pain and function perceived by patients. However, the commonly used self-report questionnaires are developed for use in general population with spinal disorders.

Research frontiers

It is necessary to use self-report questionnaires validated specifically for athletes with NP. The current research hotspot is that there is no specific test available for assessing athletes with NP. It is, therefore, necessary to develop either new self-report questionnaires or validate existing instruments for athletes with NP.

Innovations and breakthroughs

FRI is one of the commonly used self-report instrument to evaluate the patients' perspectives on their disability in general population with low back pain (LBP) as well as NP. The FRI first developed in English language is reliable, valid and responsive, and has been adapted and validated into various languages. The Persian FRI (PFRI) is previously validated for athletes with LBP. This report presents a study, for the first time, validating the PFRI in athletes with NP. The results show satisfactory psychometric properties of PFRI for use in athletes with NP.

Applications

The results of the present study demonstrated that the PFRI is reliable and valid in athletes with NP and it may be useful for assessing pain and functional status of Persian speaking athletes with NP. The equivalency of PFRI with the original English version indicates that the FRI is reliable and valid in athletes with NP, and may be used in multinational investigations as an outcome measure.

Terminology

Many athletes may experience NP due to ligament sprains, muscle strains, and contusions. The athletes with NP may complain from deficits in neck mobility, muscle recruitment, strength, endurance, or postural stability. The FRI is a quick, self-report questionnaire used to assess disability in patients with both LBP and NP. The scale contains 10 questions measuring both pain and function in a five-point scale from 0 (no pain/full function) to 4 (worst possible pain/unable to perform function). Total score calculated in percentage range between 0% and 100%, with higher scores indicating higher disability.

Peer-review

This paper is a well designed paper and gives out the result that the other scoring system can be used for evaluation for neck pain of the athletes.

REFERENCES

- 1 **Villavicencio AT**, Hernández TD, Burneikiene S, Thramann J. Neck pain in multisport athletes. *J Neurosurg Spine* 2007; **7**: 408-413 [PMID: 17933315]
- 2 **Wilber CA**, Holland GJ, Madison RE, Loy SF. An epidemiological analysis of overuse injuries among recreational cyclists. *Int J Sports Med* 1995; **16**: 201-206 [PMID: 7649713 DOI: 10.1055/s-2007-972992]
- 3 **Zmurko MG**, Tannoury TY, Tannoury CA, Anderson DG. Cervical sprains, disc herniations, minor fractures, and other cervical injuries in the athlete. *Clin Sports Med* 2003; **22**: 513-521 [PMID: 12852684 DOI: 10.1016/S0278-5919(03)00003-6]
- 4 **Michaelson P**, Michaelson M, Jaric S, Latash ML, Sjölander P, Djupsjöbacka M. Vertical posture and head stability in patients with chronic neck pain. *J Rehabil Med* 2003; **35**: 229-235 [PMID: 14582555 DOI: 10.1080/16501970306093]
- 5 **O'Leary S**, Jull G, Kim M, Vicenzino B. Cranio-cervical flexor muscle impairment at maximal, moderate, and low loads is a feature of neck pain. *Man Ther* 2007; **12**: 34-39 [PMID: 16777470 DOI: 10.1016/j.math.2006.02.010]
- 6 **Childs JD**, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, Sopyk BJ, Godes JJ, Flynn TW. Neck pain: Clinical practice guidelines linked to the International Classification of Functioning, Disability, and Health from the Orthopedic Section of the American Physical Therapy Association. *J Orthop Sports Phys Ther* 2008; **38**: A1-A34 [PMID: 18758050 DOI: 10.2519/jospt.2008.0303]
- 7 **Feise RJ**, Michael Menke J. Functional rating index: a new valid and reliable instrument to measure the magnitude of clinical change in spinal conditions. *Spine (Phila Pa 1976)* 2001; **26**: 78-86; discussion 87 [PMID: 11148650]
- 8 **Ansari NN**, Feise RJ, Naghdi S, Ebadi S, Yoosefinejad AK. The functional rating index: reliability and validity of the Persian language version in patients with low back pain. *Spine (Phila Pa 1976)* 2011; **36**: E1573-E1577 [PMID: 21270679 DOI: 10.1097/BRS.0b013e3182103282]
- 9 **Ansari NN**, Feise RJ, Naghdi S, Mohseni A, Rezazadeh M. The functional rating index: reliability and validity of the Persian language version in patients with neck pain. *Spine (Phila Pa 1976)* 2012; **37**: E844-E848 [PMID: 22310090 DOI: 10.1097/BRS.0b013e31824b5bde]
- 10 **Naghdi S**, Ansari NN, Yazdanpanah M, Feise RJ, Fakhari Z. The validity and reliability of the functional rating index for evaluating low back pain in athletes. *Scand J Med Sci Sports* 2015; **25**: 840-845 [PMID: 25809588 DOI: 10.1111/sms.12447]
- 11 **Terwee CB**, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, Bouter LM, de Vet HC. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol* 2007; **60**: 34-42 [PMID: 17161752 DOI: 10.1016/j.jclinepi.2006.03.012]
- 12 **Mousavi SJ**, Parnianpour M, Montazeri A, Mehdian H, Karimi A, Abedi M, Ashtiani AA, Mobini B, Hadian MR. Translation and validation study of the Iranian versions of the Neck Disability Index and the Neck Pain and Disability Scale. *Spine (Phila Pa*

- 1976) 2007; **32**: E825-E831 [PMID: 18091478 DOI: 10.1097/BRS.0b013e31815ce6dd]
- 13 **Farrar JT**, Young JP, LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 2001; **94**: 149-158 [PMID: 11690728 DOI: 10.1016/S0304-3959]
- 14 **Feise RJ**, Menke JM. Functional Rating Index: literature review. *Med Sci Monit* 2010; **16**: RA25-RA36 [PMID: 20110929]
- 15 **Vernon H**, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther* 1991; **14**: 409-415 [PMID: 1834753]
- 16 **Haefeli M**, Elfering A. Pain assessment. *Eur Spine J* 2006; **15** Suppl 1: S17-S24 [PMID: 16320034 DOI: 10.1007/s00586-005-1044-x]
- 17 **Terwee CB**, Dekker FW, Wiersinga WM, Prummel MF, Bossuyt PM. On assessing responsiveness of health-related quality of life instruments: guidelines for instrument evaluation. *Qual Life Res* 2003; **12**: 349-362 [PMID: 12797708]
- 18 **Ansari NN**, Naghdi S, Hasanvand S, Fakhari Z, Kordi R, Nilsson-Helander K. Cross-cultural adaptation and validation of Persian Achilles tendon Total Rupture Score. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 1372-1380 [PMID: 26740087]

P- Reviewer: Kuptmiratsaikul V, Wu WT, Yang HO **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Wu HL



Slacklining and stroke: A rehabilitation case study considering balance and lower limb weakness

Charles P Gabel, Natalie Rando, Markus Melloh

Charles P Gabel, Coolum Physiotherapy Sunshine Coast, Queensland 4573, Australia

Natalie Rando, Physiotherapy Program, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4226, Australia

Markus Melloh, Centre for Health Sciences, School of Health Professions, Zurich University of Applied, Sciences, 8400 Winterthur, Switzerland

Markus Melloh, Centre for Medical Research, University of Western Australia, Nedlands 6909, Australia

Author contributions: Charles PG performed the rehabilitation exercises with the case study patient in the clinical setting; Markus M provided vital input for the manuscript content, references and editing of the manuscript; Natalie R provided specific vital input regarding neurological rehabilitation, referencing and editing of the manuscript; all authors contributed to writing the manuscript.

Institutional review board statement: This case study was approved by the Coolum Physiotherapy Clinic through a clinical directors meeting to approve the study as part of a research initiative.

Informed consent statement: The patient has provided her informed consent.

Conflict-of-interest statement: No author has a conflict of interest for this study.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Charles P Gabel, MDT, PHD, Private Researcher, Coolum Physiotherapy Sunshine Coast, PO Box 760, Coolum Beach, Queensland 4573, Australia. cp.gabel@bigpond.com
Telephone: +61-7-54461022
Fax: +61-7-54717022

Received: January 23, 2016
Peer-review started: January 24, 2016
First decision: March 24, 2016
Revised: April 4, 2016
Accepted: June 14, 2016
Article in press: June 16, 2016
Published online: August 18, 2016

Abstract

To ascertain the effectiveness of slacklining as a supplementary therapy for elderly stroke patients who are functionally non-progressing. This case study involved an 18-mo prospective observation of the management of an 87-year-old female stroke-patient of the left hemisphere with reduced balance, reduced lower limb muscular activation, hypertonia, and concurrent postural deficits. This entailed the initial acute care phase through to discharge to home and 18-mo final status in her original independent living setting. The introduction of slacklining as an adjunct therapy was made 12 mo post incident. Slacklining involves balance retention on a tightened band where external environmental changes cause a whole-body dynamic response to retain equilibrium. It is a complex neuromechanical task enabling individualized self-developed response strategies to be learned and adapted. This facilitates the innate process of balance retention, lower-limb and core muscle activation, and stable posture through a combination of learned motor skills and neurological system down regulation. Individuals adopt and follow established sequential motor learning stages where the acquired balance skills

are achieved in a challenging composite-chain activity. Slacklining could be considered an adjunct therapy for lower limb stroke rehabilitation where function is compromised due to decreased muscle recruitment, decreased postural control and compromised balance. Initial inpatient rehabilitation involved one-month acute-care, one-month rehabilitation, and one-month transitional care prior to home discharge. A further six months of intensive outpatient rehabilitation was provided with five hourly sessions per week including: supervised and self-managed hydrotherapy, plus one individual and two group falls' prevention sessions. These were supported by daily home exercises. At 12 mo post incident, recovery plateaued, then regressed following three falls. Rehabilitation was subsequently modified with the hydrotherapy retained and the group sessions replaced with an additional individual session supplemented with slacklining. The slacklining followed stages one and two of a standardized five-stage protocol. Self-reported functional progression resumed with improvement by 14 mo which further increased and was sustained 18 mo (Students' *t* test $P < 0.05$). Slacklining's external stimulations activate global-body responses through innate balance, optimal postural and potentially down-regulated reflex control. Incorporated into stroke rehabilitation programs, slacklining can provide measurable functional gains.

Key words: Stroke; Rehabilitation; Lower limbs; Balance; Slacklining

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Slacklining may supplement stroke rehabilitation where lower limb function is compromised. This case study considers an 87-year-old female with reduced balance, reduced lower limb activation, and hypertonia. Rehabilitation from acute care to home discharge and subsequent six-month intensive outpatient therapy showed progression then plateaued at nine months. Three falls resulted in regression and rehabilitation was modified by supplementing slacklining. Functional progression improved by 14 mo and was sustained at 18 mo. Slacklining's external stimulations activate global-body responses through innate balance, optimal postural response and potentially down-regulated reflex control that can provide quantifiable functional gains. Further prospective cohort studies are required.

Gabel CP, Rando N, Melloh M. Slacklining and stroke: A rehabilitation case study considering balance and lower limb weakness. *World J Orthop* 2016; 7(8): 513-518 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i8/513.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i8.513>

INTRODUCTION

Stroke survivors are often required to adapt to a

restricted lifestyle with reduced activities of daily living (ADL). They also have increased dependence on continuous external support to survive^[1]. Thirty-five per-cent of Australians who experienced a stroke had a resulting disability, with 64% needing assistance with health care, 58% with mobility and 47% with self-care^[2]. Furthermore, this neurologic pathology significantly impacts the ADL of individuals through impaired postural control. Following stroke, some patients have delayed and disrupted equilibrium reactions^[3], exaggerated postural sway in both sagittal and frontal planes^[4], reduced weight-bearing on the paretic limb during functional tasks^[5,6] and an increased risk of falling^[7,8].

Additionally, impaired dexterity in both the affected and unaffected lower extremities is a major reported problem post-stroke^[9]. Activation failure in the affected lower limb can often be explained by weakness, which correlates strongly with reduced functional performance^[7]. Furthermore, the presence of co-activation, muscle activation on both sides of the joint, is a common postural coordination strategy reported in those with neurologic deficits, including stroke^[10]. Consequently, research is required for post-stroke rehabilitation strategies that focus strongly on improving the affected lower limb's dexterity and postural control. One such novel technique not yet reported in the literature is slacklining as a supplementary therapy^[11-14]. It is a complex neuromechanical task that involves balance retention on a tightened band where whole-body dynamics drive the response to external environmental changes^[13,15]. This activity innately facilitates recruitment of muscles within the core^[11,16] and the lower limb, particularly the quadriceps and gluteals^[12]. Some studies have found that slacklining has transferable learning and skill acquisition including improved posture^[14,17], static and dynamic balance^[18-20], lower limb control^[12,21,22], joint specific control^[12,23,24], sporting performance^[13,25] and probable neuroplastic changes^[26,27]. Slacklining also stimulates the balance mechanism and functional control through individualized global body responses and learned movement patterns that are adaptations to external stimuli^[15,17,22].

This paper presents a case study where slacklining was supplemented to an existing balance and functional control rehabilitation program.

CASE REPORT

An 87-year-old female who had sustained a non-specific cerebro-vascular accident within the left hemisphere affecting lower limb strength, balance control and hypertonia was monitored over an 18 mo period. Rehabilitation was progressed through five stages: (1) an initial one month of acute inpatient management; (2) one month inpatient rehabilitation at a specialized rehab centre; (3) one month of transitional care in a different inpatient facility to assist home skills for self-care and daily living; (4) home discharge with nine-month

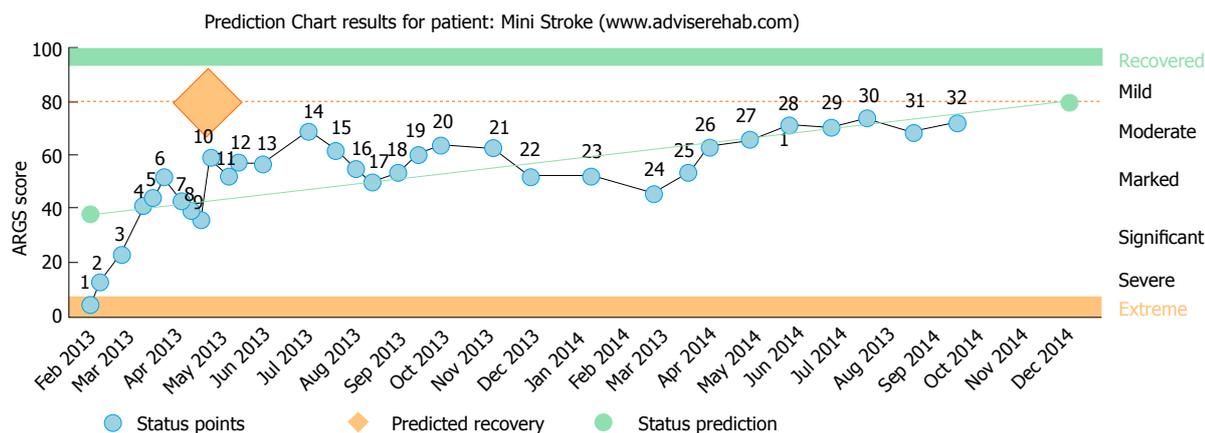


Figure 1 Visual history of recovery stages. ARGS: Advise Rehab Global Score.

early care community support through nursing and carers; plus five times per week intensive outpatient rehabilitation involving hourly sessions of twice weekly occupational and physical therapy group falls prevention, an individual physical therapy session providing balance training, mobilization and massage with planning of additional home exercise, and two hydrotherapy sessions; and (5) management in the community for a further six months with modification of the outpatient sessions combined with the introduction of slacklining and a phase out of regular home care assistance. Slacklining, as part of the neurological rehabilitation program, was introduced and initially graduated over six weeks following the standardized protocol^[12,13]. The sessions were initiated at three minutes and increased to seven and, finally, ten minutes in duration. They involved a step up onto the slackline, located over a grassy surface at a height of approximately 20 cm, with the patient provided balance support, initially from the front with both hands touching or holding the therapists hands and progressing to a hand support such as a wheeled frame or a walking stick (Figure 1). The adjunct or supplementary addition of slacklining to the standard rehabilitation program continued after the case study observation period finished at 18 mo. Sessions were twice weekly with minor progressions in the program difficulty levels based upon the individual's adaptations, capacity and status (Figure 2).

The status and the key points were recorded using computerized decision support software patient-reported outcome measurement^[28] (Figure 1). Recovery plateaued at the six-month mark and there was subsequent regression following three falls at home over the subsequent six months despite the specific falls prevention program. At twelve-months the hydrotherapy continued and the group rehabilitation falls prevention program was ceased and replaced by a further individual rehabilitation session that was supplemented with slacklining (Figure 1). The slacklining was provided with the intention of specifically activating the quadriceps^[12,22] and improving core muscle recruitment^[14,19], postural position and

awareness^[14,17], and balance^[18,21]. The slacklining followed stages one and two of a standardized five-stage, 20-step protocol^[13]. This standard protocol was modified through the initial use of hand support that was progressively withdrawn. Initially a bilateral, two hand support position was provided, then progressed to a single hand, then one hand support to a fixed ground object, then a walking stick and finally free-standing and stepping up. At all times immediate close support was available for safety, feedback and confidence. Subsequently, functional status progression resumed with statistically significant improvement over the following six months (Students' *t* test $P < 0.05$) (Figure 2).

DISCUSSION

Slacklining has an innate or automatic muscle recruitment action, particularly for the quadriceps and to a lesser degree the gluteals, calf and core^[12,14]. These actions provide a positive focus for stroke patients with local muscle inhibition from the centrally derived deficits^[12].

A further consideration is that the action of standing on a slackline requires muscular recruitment in a sequential and learned manner in order for the individual to remain upright and balanced^[12,17]. This is a postural benefit for individuals with lower limb functional deficits of a central source that are acquired following stroke^[29,30]. An additional benefit is that the Hoffman's reflex (H-reflex)^[12,31] can be affected through the pre-synaptic pathway^[17] resulting in a learned activity that inhibits the reflex action from down regulation^[32,33]. Such inhibition is advantageous as the H-reflex shows heightened sensitivity that may negatively affect the gait of stroke survivors^[34,35]. However, it is considered to be a learned and temporary effect as withdrawal of the training stimulus results in reduction the training effect. Consequently, the effectiveness of the slacklining program as a rehabilitation therapy must be maintained through the ongoing practice of the activity^[11,13,18].

This is of significance as the stroke patient has phase-related modulation of both the soleus H-reflex,



Figure 2 Right lower limb affected stroke patient participating in Slackline balance training. A: Therapist assist - single stick; B: Patient 1 leg stand with no balance aids - therapist standby assist.

that affects the ankle directly and less so the knee - regardless of joint stiffness^[29]; and the quadriceps H-reflex primarily affecting the knee control^[31]. Both of these actions are also partially disordered during hip movement due to modulated limb spasticity^[34,35]. The anticipated beneficial consequence is that the action of slacklining may provide a positive effect through the action of pre-synaptic inhibition and down-regulation of the H-reflex^[27] as well as supplement the quadriceps and soleus activation and control^[12] in conjunction with balance, postural control, and an overall learning process^[14,18,24]. This can assist the individual to adapt towards normalized balance and actively controlled positions^[36]. The anticipation is that this specific action within the training phase will then overflow to normal daily activity^[17,18] including the functional movements of walking and postural control. This in theory could subsequently improve the innate response action to perturbations and reduce the incidence of falls and in turn improve individual confidence while reducing health and socioeconomic costs^[36].

It is widely accepted that the central nervous system of adult human beings has enormous potential for recovery and adaptability. The actions of slacklining can theoretically cause down-regulation of the muscle inhibitory action and the Hoffman reflex. This suppression of a spinal reflex may transfer the control of muscular activation from primary spinal to more supraspinal centers, which can be beneficial in terms of improved movement control^[37,38]. Consequently, slacklining and its potential to influence cortical areas and the central nervous system of stroke patients is an area that needs investigation in this population group^[34,35].

Slacklining may be a beneficial rehabilitation method that could be incorporated into the programs of stroke patients. The external stimuli activate global-body responses through innate balance and reflex modulations that provide quantifiable functional gains. In addition, the activity of slacklining provides an

innate activation of the lower limb muscles, particularly the quadriceps, calf, gluteals and also the trunk core muscles in normal and lower limb injured individuals; consequently, it would seem likely to have a similar effect in stroke patients. Slacklining is a novel adjunct therapy that is challenging and rewarding where quantifiable exercise specific gains can be achieved and potentially transformed into daily functional status improvements in the areas of ADL, gait and balance. Further prospective studies are required to validate these initial findings and eventually to determine therapy frequency and progression rates.

COMMENTS

Case characteristics

An 87-year-old female stroke patient is discussed within the context of a novel method of rehabilitation through the use of slacklining to facilitate balance and function and to reduce and prevent falls.

Clinical diagnosis

Right lower limb weakness, mildly reduced sensation, reduced balance and general limb control with tonal changes and intermittent upper limb tonal alterations to a mild level.

Differential diagnosis

Stroke affecting the right leg below the knee due to a left cerebral vascular accident (CVA).

Treatment

A progressive graded rehabilitation over 18 mo from inpatients to transitional care and final home and community including a group falls reduction program. Progression to twice weekly physiotherapy outpatients with balance training, limb mobilization and massage and the addition of slacklining.

Term explanation

Stroke is due to a CVA affecting the cortical tissue and slacklining as a novel therapy involves balance retention on a tightened band where external environmental changes cause a whole-body dynamic response to retain equilibrium. As such slacklining is a complex neuromechanical task enabling individualized self-developed response strategies to be learned and adapted to

facilitate balance, strength, control and functional improvement and/or stability.

Experiences and lessons

This study offers a new frontier into the use of neural plasticity accessed through physical rehabilitation exercises to enhance and maintain balance and function. This is the first reported study with the use of this novel method of rehabilitation, "slacklining", in a clinical setting for stroke.

Peer-review

This paper proposes the activity 'Slacklining' as a rehabilitation supplement following stroke in the form of a case report and theoretical explanation. The manuscript is well written, and supported by references appropriately.

REFERENCES

- 1 **Truelsen T**, Begg S, Mathers C. The global burden of cerebrovascular disease Geneva, World Health Organisation. Geneva: WHO, 2006: 67
- 2 **Australian Institute of Health and Welfare (AIHW)**. Stroke and its management in Australia: an update. Canberra: AIHW, 2013: 150
- 3 **Badke MB**, Duncan PW. Patterns of rapid motor responses during postural adjustments when standing in healthy subjects and hemiplegic patients. *Phys Ther* 1983; **63**: 13-20 [PMID: 6849002]
- 4 **Genthon N**, Rougier P, Gissot AS, Froger J, Pélissier J, Pérennou D. Contribution of each lower limb to upright standing in stroke patients. *Stroke* 2008; **39**: 1793-1799 [PMID: 18369174 DOI: 10.1161/STROKEAHA.107.497701]
- 5 **Engardt M**, Olsson E. Body weight-bearing while rising and sitting down in patients with stroke. *Scand J Rehabil Med* 1992; **24**: 67-74 [PMID: 1604264]
- 6 **Chou SW**, Wong AM, Leong CP, Hong WS, Tang FT, Lin TH. Postural control during sit-to stand and gait in stroke patients. *Am J Phys Med Rehabil* 2003; **82**: 42-47 [PMID: 12510184]
- 7 **Horstman AM**, Beltman MJ, Gerrits KH, Koppe P, Janssen TW, Elich P, de Haan A. Intrinsic muscle strength and voluntary activation of both lower limbs and functional performance after stroke. *Clin Physiol Funct Imaging* 2008; **28**: 251-261 [PMID: 18355344 DOI: 10.1111/j.1475-097X.2008.00802.x]
- 8 **Kerse N**, Parag V, Feigin VL, McNaughton H, Hackett ML, Bennett DA, Anderson CS. Falls after stroke: results from the Auckland Regional Community Stroke (ARCOS) Study, 2002 to 2003. *Stroke* 2008; **39**: 1890-1893 [PMID: 18483413 DOI: 10.1161/STROKEAHA.107.509885]
- 9 **Kiyama R**, Fukudome K, Hiyoshi T, Umemoto A, Yoshimoto Y, Maeda T. The loss of dexterity in the bilateral lower extremities in patients with stroke. *J Appl Biomech* 2011; **27**: 122-129 [PMID: 21576720]
- 10 **Lamontagne A**, Richards CL, Malouin F. Coactivation during gait as an adaptive behavior after stroke. *J Electromyogr Kinesiol* 2000; **10**: 407-415 [PMID: 11102843 DOI: 10.1016/S1050-6411(00)00028-6]
- 11 **Gabel CP**. Slacklining: A Novel Exercise to Enhance Quadriceps Recruitment, Core Strength and Balance Control. *J Nov Physiother* 2014; **4**: 4 [DOI: 10.4172/2165-7025.1000229]
- 12 **Gabel CP**, Osborne J, Burkett B. The influence of 'Slacklining' on quadriceps rehabilitation, activation and intensity. *J Sci Med Sport* 2015; **18**: 62-66 [PMID: 24373899 DOI: 10.1016/j.jsams.2013.11.007]
- 13 **Gabel CP**, Mendoza S. "Slacklining" - a self-generated, graded training program for lower limb rehabilitation. *IJATT* 2013; **18**: 14-19
- 14 **Pfusterschmied J**, Buchecker M, Keller M, Wagner H, Taube W, Müller E. Supervised slackline training improves postural stability. *Eur J Sports Sc* 2013; **13**: 49-57 [DOI: 10.1080/17461391.2011.583991]
- 15 **Paoletti P**, Mahadevan L. Balancing on tightropes and slacklines. *J R Soc Interface* 2012; **9**: 2097-2108 [PMID: 22513724 DOI: 10.1098/rsif.2012.0077]
- 16 **Anlauff J**, Cooperstock JR, Fung J. Augmented feedback for learning single-legged stance on a slackline. Philadelphia: International Conference on Virtual Rehabilitation (ICVR), 2013: 162-163 [DOI: 10.1109/ICVR.2013.6662104]
- 17 **Keller M**, Pfusterschmied J, Buchecker M, Müller E, Taube W. Improved postural control after slackline training is accompanied by reduced H-reflexes. *Scand J Med Sci Sports* 2012; **22**: 471-477 [PMID: 21385217 DOI: 10.1111/j.1600-0838.2010.01268.x]
- 18 **Granacher U**, Iten N, Roth R, Gollhofer A. Slackline training for balance and strength promotion. *Int J Sports Med* 2010; **31**: 717-723 [PMID: 20677124 DOI: 10.1055/s-0030-1261936]
- 19 **Mahaffey BJ**. The Physiological Effects Of Slacklining On Balance And Core StrengthPhysical Education Teaching, University of Wisconsin-La Crosse. Crosse: University of Wisconsin-La Crosse, 2009: 62
- 20 **Seeber G**, Zalpour C. Auswirkungen des Slacklinings "auf die Gleichgewichtsfähigkeit von Senioren. *Prävention und Gesundheitsförderung* (German) 2012; **7**: 30-35 [DOI: 10.1007/s11553-011-0318-x]
- 21 **Pfusterschmied J**, Lindinger S, Buchecker M, Stöggel T, Wagner H, Müller E. Effect of instability training equipment on lower limb kinematics and muscle activity. *Sportverletz Sportschaden* 2013; **27**: 28-33 [PMID: 23404457 DOI: 10.1055/s-0032-1330725]
- 22 **Pfusterschmied J**, Stöggel T, Buchecker M, Lindinger S, Wagner H, Müller E. Effects of 4-week slackline training on lower limb joint motion and muscle activation. *J Sci Med Sport* 2013; **16**: 562-566 [PMID: 23333134 DOI: 10.1016/j.jsams.2012.12.006]
- 23 **Mayer C**, Siems W. *Patellaluxation 100 Krankheitsbilder in der Physiotherapie*. Berlin: Springer Berlin Heidelberg, 2011: 146-157 [DOI: 10.1007/978-3-642-17267-0_15]
- 24 **Di Stasi S**, Myer GD, Hewett TE. Neuromuscular training to target deficits associated with second anterior cruciate ligament injury. *J Orthop Sports Phys Ther* 2013; **43**: 777-792, A1-11 [PMID: 24175599 DOI: 10.2519/jospt.2013.4693]
- 25 **De Franceschi PA**. Le slackline, un outil prophylactique au service des joueurs de badminton de haut niveau, France, 2012: 12
- 26 **Sibley KM**, Salbach NM. Applying knowledge translation theory to physical therapy research and practice in balance and gait assessment: case report. *Phys Ther* 2015; **95**: 579-587 [PMID: 24970093 DOI: 10.2522/ptj.20130486]
- 27 **Zehr EP**. Considerations for use of the Hoffmann reflex in exercise studies. *Eur J Appl Physiol* 2002; **86**: 455-468 [PMID: 11944092 DOI: 10.1007/s00421-002-0577-5]
- 28 **Advise Rehab Advise Rehabilitation, decision support software**. Coolum Beach, Queensland: Advise rehabilitation Pty Ltd, 2013
- 29 **Harburn KL**, Vandervoort AA, Helewa A, Goldsmith CH, Kertesz A, Teasell RW, Hill KM. A reflex technique to measure presynaptic inhibition in cerebral stroke. *Electromyogr Clin Neurophysiol* 1995; **35**: 149-163 [PMID: 7649061]
- 30 **Yavuzer G**, Eser F, Karakus D, Karaoglan B, Stam HJ. The effects of balance training on gait late after stroke: a randomized controlled trial. *Clin Rehabil* 2006; **20**: 960-969 [PMID: 17065539 DOI: 10.1177/0269215506070315]
- 31 **Hopkins JT**, Wagie NC. Intrasession and intersession reliability of the quadriceps Hoffmann reflex. *Electromyogr Clin Neurophysiol* 2003; **43**: 85-89 [PMID: 12661132]
- 32 **Van Boxtel A**. Differential effects of low-frequency depression, vibration-induced inhibition, and posttetanic potentiation on H-reflexes and tendon jerks in the human soleus muscle. *J Neurophysiol* 1986; **55**: 551-568 [PMID: 3514814]
- 33 **Schneider C**, Lavoie BA, Capaday C. On the origin of the soleus H-reflex modulation pattern during human walking and its task-dependent differences. *J Neurophysiol* 2000; **83**: 2881-2890 [PMID: 10805685]
- 34 **Tanabe S**, Kamiya A, Muraoka Y, Masakado Y, Tomita Y. Disorder of phase-related modulation of soleus H-reflex during hip movement in stroke patients. *Electromyogr Clin Neurophysiol* 2006; **46**: 241-246 [PMID: 16929631]
- 35 **Tanabe S**, Muraoka Y, Kamiya A, Tomita Y, Masakado Y. Passive movement of hip and knee joints decreases the amplitude of soleus H-reflex in stroke patients. *Electromyogr Clin Neurophysiol* 2004;

Gabel CP *et al.* Slacklining for stroke rehabilitation

44: 365-370 [PMID: 15473349]

- 36 **Hoffman J**, Gabel P. Expanding Panjabi's stability model to express movement: a theoretical model. *Med Hypotheses* 2013; **80**: 692-697 [PMID: 23561576 DOI: 10.1016/j.mehy.2013.02.006]
- 37 **Solopova IA**, Kazennikov OV, Deniskina NB, Levik YS, Ivanenko YP. Postural instability enhances motor responses to transcranial

magnetic stimulation in humans. *Neurosci Lett* 2003; **337**: 25-28 [PMID: 12524163 DOI: 10.1016/S0304-3940(02)01297-1]

- 38 **Taube W**, Gruber M, Gollhofer A. Spinal and supraspinal adaptations associated with balance training and their functional relevance. *Acta Physiol (Oxf)* 2008; **193**: 101-116 [PMID: 18346210 DOI: 10.1111/j.1748-1716.2008.01850.x]

P- Reviewer: Anand A, Kwasnicki RM, Sakamoto A **S- Editor:** Qiu S

L- Editor: A **E- Editor:** Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 September 18; 7(9): 519-627



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 328 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (16), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tajchung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarng, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Moraes Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*

Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srečko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*
 Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efstathios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*

Keith Baldwin, *Philadelphia*
 Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort San Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*



REVIEW

- 519 Return to sports after shoulder arthroplasty
Johnson CC, Johnson DJ, Liu JN, Dines JS, Dines DM, Gulotta LV, Garcia GH
- 527 Management of Ewing sarcoma family of tumors: Current scenario and unmet need
Biswas B, Bakhshi S

MINIREVIEWS

- 539 Casting: Pearls and pitfalls learned while caring for children's fractures
Nguyen S, McDowell M, Schlechter J
- 546 Implant retention after acute and hematogenous periprosthetic hip and knee infections: Whom, when and how?
Triantafyllopoulos GK, Soranoglou V, Memsoudis SG, Poultsides LA

ORIGINAL ARTICLE

Retrospective Cohort Study

- 553 Surgical treatment of Lenke 5 adolescent idiopathic scoliosis: Comparison of anterior vs posterior approach
Abel MF, Singla A, Feger MA, Sauer LD, Novicoff W

Observational Study

- 561 Attitudes and diagnostic practice in low back pain: A qualitative study amongst Greek and British physiotherapists
Billis E, McCarthy CJ, Gliatis J, Matzaroglou C, Oldham JA

- 570 Epidemiology of isolated hand injuries in the United Arab Emirates
Grivna M, Eid HO, Abu-Zidan FM

Prospective Study

- 577 Risk assessment instruments for screening bone mineral density in a Mediterranean population
Christodoulou S, Drosos GI, Ververidis A, Galanos A, Anastassopoulos G, Kazakos K

SYSTEMATIC REVIEWS

- 584 Total knee arthroplasty for treatment of post-traumatic arthritis: Systematic review
Saleh H, Yu S, Vigdorchik J, Schwarzkopf R

- 592 Biologic agents for anterior cruciate ligament healing: A systematic review

Di Matteo B, Loibl M, Andriolo L, Filardo G, Zellner J, Koch M, Angele P

- 604 Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review

Janssen RPA, Reijman M, Janssen DM, van Mourik JBA

CASE REPORT

- 618 Compartment syndrome following total knee replacement: A case report and literature review

Shaath M, Sukeik M, Mortada S, Masterson S

- 623 Lateral subtalar dislocation: Case report and review of the literature

Veltman ES, Steller EJA, Wittich P, Keizer J

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Sergio Hernandez-Sanchez, MSc, Physiotherapist, Professor, Physiotherapy Area, Pathology and Surgery Department, Faculty of Medicine, Miguel Hernandez University, 03550 Sant Joan D'alacant, Spain

AIM AND SCOPE

World Journal of Orthopedics (World J Orthop, WJO, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central and Scopus.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Dan Li*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL BOARD MEMBERS
 All editorial board members resources online at <http://www.wjgnet.com>

www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
 Xiu-Xia Song, Director
 Fang-Fang Ji, Vice Director
World Journal of Orthopedics
 Baishideng Publishing Group Inc
 8226 Regency Drive, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLICATION DATE
 September 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>

Return to sports after shoulder arthroplasty

Christine C Johnson, Daniel J Johnson, Joseph N Liu, Joshua S Dines, David M Dines, Lawrence V Gulotta, Grant H Garcia

Christine C Johnson, Joseph N Liu, Joshua S Dines, David M Dines, Lawrence V Gulotta, Grant H Garcia, Department of Sports Medicine and Shoulder Surgery, Hospital for Special Surgery, New York, NY 10021, United States

Daniel J Johnson, the School of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232, United States

Author contributions: All authors contributed to the preparation and submission of this work.

Conflict-of-interest statement: The following authors declared potential conflicts of interest: Dines JS is a paid consultant for Arthrex and Conmed; Dines DM receives royalties from Biomet; Gulotta LV is a paid consultant for Biomet.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Christine C Johnson, MD, Department of Sports Medicine and Shoulder Surgery, Hospital for Special Surgery, 535 E 70th St, New York, NY 10021, United States. johnsonc@hss.edu
 Telephone: +1-212-6061466
 Fax: +1-212-6061477

Received: March 20, 2016
 Peer-review started: March 23, 2016
 First decision: April 20, 2016
 Revised: April 30, 2016
 Accepted: June 27, 2016
 Article in press: June 29, 2016
 Published online: September 18, 2016

Abstract

Many patients prioritize the ability to return to sports

following shoulder replacement surgeries, including total shoulder arthroplasty (TSA), reverse total shoulder arthroplasty (RTSA), and hemiarthroplasty (HA). While activity levels after hip and knee replacements have been well-established in the literature, studies on this topic in the field of shoulder arthroplasty are relatively limited. A review of the literature regarding athletic activity after shoulder arthroplasty was performed using the PubMed database. All studies relevant to shoulder arthroplasty and return to sport were included. The majority of patients returned to their prior level of activity within six months following TSA, RTSA, and shoulder HA. Noncontact, low demand activities are permitted by most surgeons postoperatively and generally have higher return rates than contact sports or high-demand activities. In some series, patients reported an improvement in their ability to participate in sports following the arthroplasty procedure. The rates of return to sports following TSA (75%-100%) are slightly higher than those reported for HA (67%-76%) and RTSA (75%-85%). Patients undergoing TSA, RTSA, and shoulder HA should be counseled that there is a high probability that they will be able to return to their preoperative activity level within six months postoperatively. TSA has been associated with higher rates of return to sports than RTSA and HA, although this may reflect differences in patient population or surgical indication.

Key words: Total shoulder arthroplasty; Reverse total shoulder arthroplasty; Shoulder replacement; Return to sport; Hemiarthroplasty

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Many patients prioritize the ability to return to sports following shoulder replacement surgeries, including total shoulder arthroplasty, reverse total shoulder arthroplasty and hemiarthroplasty. While activity levels after hip and knee replacements have been well-established in the literature, studies on this topic in the field of shoulder arthroplasty are relatively limited. Information about activity levels and the rate of return

to sports following shoulder arthroplasty would help both patients and surgeons more accurately manage expectations. This clinical review examines how return to sport following shoulder arthroplasty has been studied and reported in the literature.

Johnson CC, Johnson DJ, Liu JN, Dines JS, Dines DM, Gulotta LV, Garcia GH. Return to sports after shoulder arthroplasty. *World J Orthop* 2016; 7(9): 519-526 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/519.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.519>

INTRODUCTION

Over the past decade, shoulder replacement surgeries, including total shoulder arthroplasty (TSA), reverse total shoulder arthroplasty (RTSA), and hemiarthroplasty (HA), have become increasingly more common^[1,2]. Technical innovations in shoulder arthroplasty have led to good implant survival and satisfactory long-term outcomes^[3-6]. Although most commonly performed in elderly patients for degenerative shoulder conditions^[3-5,7], shoulder replacement surgery is also routinely performed in young and active patients^[8-11].

As the indications for these procedures expand and life expectancy increases, the goals of shoulder replacement are changing, and many patients are now prioritizing the ability to resume sports postoperatively^[12-15]. Frequently during both preoperative and follow-up visits, patients inquire about sports after shoulder arthroplasty^[12]. While activity levels after hip and knee replacements have been extensively reported in the literature^[16-23], the number of studies on this topic in the field of shoulder arthroplasty are relatively limited^[13,14].

Information about activity levels and the rate of return to sports following shoulder arthroplasty would help both patients and surgeons more accurately manage expectations^[24]. This clinical review examines how return to sport following shoulder arthroplasty has been studied and reported in the literature^[12].

RETURN TO SPORT AFTER TSA

TSA has been shown to be a highly effective treatment for degenerative shoulder disease, and has been shown to have good medium- and long-term outcomes^[7,25,26]. The number of total shoulder arthroplasties performed in the United States has risen exponentially over the last decade: Since 2004, TSA has increased by approximately 3000 cases each year in the United States compared with an annual increase of fewer than 400 cases each year prior^[27]. This trend is only expected to continue^[27], and patients have come to have higher expectations of their functions postoperatively. While return to activity has been studied extensively in the lower extremity arthroplasty literature, it is only relatively recently that the same focus has been

placed on TSA^[12-14].

The largest study by Bühlhoff *et al.*^[28] examined return to sports in 154 TSA patients at an average follow-up of 6.2 years. Their cohort included 105 TSA patients who had participated in sports preoperatively (group 1) and 49 TSA patients who had never participated in sports (group 2). At the time of final follow-up, 60 patients (39%) were participating in sports, and all 60 patients were from the first group (those that had participated in sports preoperatively). The authors concluded that patients who had not recently participated in sports are unlikely to do so after surgery. Among patients who had participated in sports preoperatively, however, the rate to return to sports was 57% in their cohort. Furthermore, of the 45 patients who participated in sports preoperatively and did not resume the activity postoperatively, only 18% cited shoulder problems as the reason^[28].

McCarty *et al.*^[13] reported on 75 patients (86 shoulders) with a minimum follow-up of two years. In their series, 54 patients (61 shoulders) underwent TSA and the other 21 patients (25 shoulders) received a HA. Sixty-four percent of the patients stated that one of the reasons that they were having the surgery was to participate in sports. Overall, 81% of patients resumed at least one sport following the arthroplasty procedure, and 71% of these patients demonstrated an improvement in their ability to play the sport. In their study, fishing (92%), swimming (86%), and golf (77%) were associated with the highest rates of return postoperatively; bowling (40%) and softball (20%) showed the least favorable rates of return. Patients participated in their sport more frequently after surgery (1.7 d/wk compared to 0.7 d/wk previously), and most made a full return to sports by 5.8 mo postoperatively.

Zarkadas *et al.*^[1] used a mailed questionnaire to assess patient-reported activity after either TSA or HA. With respect to the TSA group, 27 of the 52 respondents (60%) reported having high demand use of their shoulder. The most commonly reported sports that patients were unable to perform due to the arthroplasty procedure were canoeing, biking, and golf^[1].

Schmidt-Wiethoff *et al.*^[29] reported that 62 of 74 patients (84%) were able to return to sport after TSA, but 30% (19 patients) played with limitations. The remaining 12 patients (16%) did not return to sports, but it is not known whether this was due to shoulder problems or comorbid medical conditions^[12,29,30].

Schumann *et al.*^[15] reported on 100 patients who underwent TSA and were followed for a minimum of one year. Eighty-nine percent of patients who participated in sports preoperatively (49 of 55) were able to resume participating in that sport at an average follow-up of 2.8 years; over a third of these patients (36.7%), however, reported persistent restrictions on sports activities due to shoulder issues. Regarding time to return to sports, 67% of the patients that resumed sports were able to do so within 6 mo. Golf was one of the most commonly reported sporting activity in their series (16.3%), and many of the golfers reported an improvement in performance

postoperatively: The golfers in their series increased their maximum drive distance from an average of 110 ± 91.5 m preoperatively to an average of 173.1 ± 51.2 m following the arthroplasty procedure.

Jensen *et al.*^[14] studied 24 patients (26 shoulders) who played golf prior to TSA (20 shoulders) or HA (6 shoulders). They found that all but 1 patient (96%) had returned to golf by a mean of 4.5 mo postoperatively. Performance improved in most patients, and 18 patients were able to decrease their handicap by an average of five strokes postoperatively. When compared to 76 non-golf playing controls, golfers did not have an increased risk of implant loosening at an average follow-up of 52.4 mo^[14].

In summary, these studies demonstrate that patients who participate in sports preoperatively have a high likelihood of returning to sports after TSA. Most are able to return to full activity within six months, and some patients will experience an improvement in their performance. Patients should be cautioned that a small proportion of patients report persistent restrictions on sports activities following TSA.

RETURN TO SPORT AFTER REVERSE TSA

In 2003, the reverse prosthesis, or RTSA, was approved by the Food and Drug Administration for patients with cuff tear arthropathy^[31]. Despite the technical challenges it initially presented to surgeons^[32], the results of RTSA have been encouraging^[31,33], and the indications for RTSA have expanded to include proximal humerus fractures and TSA revisions^[24]. The success of the reverse total shoulder prosthesis has been shown to contribute to the large increase in the number of shoulder replacement procedures performed in the United States over the past decade^[2,34,35]. Reverse prostheses accounted for nearly half of all total shoulder arthroplasties performed in 2011^[36]. Patient satisfaction has been shown to correlate with the resumption of recreational activities^[37,38], but only a handful of studies have assessed return to sport and activity following RTSA.

Edwards *et al.*^[39] reported on postoperative activity levels in a small number ($n = 4$) of RTSA patients. The authors found that 75% of the patients in this series returned to preoperative sports.

Lawrence *et al.*^[40] surveyed 78 RTSA patients (81 shoulders) at an average follow-up of 3.6 years, and found that they maintained a high level of activity following RTSA. The most commonly reported low-demand sporting activities were stationary biking (31%) and treadmill (23%), and the most popular medium-demand sports were fishing (23%), dancing (16%), and swimming (16%). The authors concluded that the activities patients participate in after RTSA are similar to those reported after other types of shoulder arthroplasty, including TSA and HA.

In an evaluation of RTSA in a senior athletic popu-

lation, Simovitch *et al.*^[41] reported that 60% (40 of 67) patients who participated in a sport preoperatively returned to sports after surgery. Of the patients that resumed sports postoperatively, 12 patients (30%) indicated that they were able to perform their activities at a higher level, and 26 patients (65%) reported no change in performance. The three most popular sports in their series were golf, swimming, and water aerobics. The authors also examined radiographic outcomes in the patients who returned to sports for a minimum of 35 mo (mean 43 mo). At final follow-up, a single zone of lucency was present in 17% of humeral stems and there was one case of early subsidence, but no cases with loosening. The glenoid notching rate was 7% in their cohort, but there were no cases of glenoid subsidence, lucency, or loosening.

Garcia *et al.*^[24] reported on 76 RTSA patients at an average follow-up of 31.6 mo. All of the patients included in their series participated in sports preoperatively, and the authors found that 85.5% of patients returned to at least one sport following RTSA. The average time to return to full sport was 5.3 mo. The sports with the highest rates of return included fitness sports (81.5%), swimming (66.7%), running (57.1%), cycling (50%), and golf (50%). Nearly half (47.6%) of the patients reported that the duration and intensity of their sporting activities had increased. The most common reasons for not returning to sports in their series were pain (13.1%), shoulder issues related to surgery (11.8%), and loss of interest (9.2%).

Despite no clear consensus in the literature regarding the acceptable activity level after RTSA, the available data demonstrates that most patients are able to return to low-impact sports, such as swimming, biking, jogging, and golf. Further studies are required to determine the mid- and long-term impact of increased activity and load-bearing following RTSA.

RETURN TO SPORT AFTER HA

Despite exponential rises in TSA and RTSA, the rate of HA procedures continues to grow^[2]. Glenohumeral HA is well established as a method to treat glenohumeral arthritis and complex three- and four-part proximal humerus fractures^[42]. With its low failure rate, HA has traditionally been considered a safer option than total or reverse total shoulder replacements for patients who wish to remain active^[41]. Other advantages of HA over these other prostheses include a less technically demanding procedure and shorter operative time^[43]. However, others caution against its use in young, active patients, as long-term data shows deteriorating outcomes and worsening glenoid erosion for shoulders that undergo HA for osteoarthritis^[44]. Despite a relative indication for HA in patients who wish to resume sporting activities^[45], there is limited data on rates of return to sports after HA.

Skutek *et al.*^[46] evaluated a small series ($n = 13$) of HA patients and reported a 76% rate of return to

preoperative sport. Swimming ($n = 6$) and cycling ($n = 3$) were the most common sports resumed postoperatively, and the average time to return to sport was 33 wk in their series.

Garcia *et al.*^[45] reported on activity levels following HA in 79 patients at a mean follow-up of 63.1 mo. Of the 58 patients who played a sport preoperatively, the authors found that 67.2% resumed at least one of their previous sports following HA. The average time to return to full sports was 6.5 mo. Among the patients with preoperative sports participation, the sports with the highest rates of return were fitness sports (69%), swimming (65%), running (64%), cycling (63%), and doubles tennis (57%). Of the patients who returned to sports postoperatively, 87% felt that their sports outcome was good or excellent.

Return to sports after HA is considered "safer" than total or reverse shoulder arthroplasty due to its a low risk of component failure or loosening^[47]. However, the rates of return to sports following HA (67% to 76%)^[45,46] reported in the literature appears slightly lower than those reported for TSA (75%-100%)^[13-15] and RTSA (75%-85%)^[24,39]. In addition, many studies have shown poor results in long-term follow-up of HA, with one finding that only 25% of HA patients were satisfied with their outcome seventeen years after the operation^[44]. Despite these results, HA continues to be a common procedure performed by recent orthopaedic residency graduates, where it is commonly performed on younger, active patients^[48].

COMPARISON BETWEEN RETURN TO SPORT IN HA AND TSA

Patients with primary glenohumeral osteoarthritis may be treated with either TSA or HA. The choice is guided primarily by the presence or absence of glenoid arthrosis, but also in part by the patient's age and intended level of activity. TSA has been shown to provide superior pain relief, function, range of motion, and patient satisfaction as compared to HA^[49-51]. However, proponents of shoulder HA argue that it provides reliable pain relief in a shorter, less technically demanding, and less costly procedure. Furthermore, many shoulder surgeons permit patients to return to sports with less restrictions following HA as compared to TSA^[52,53]. Opposition to TSA in young active patients stems from concerns regarding implant longevity and glenoid loosening^[49]. To date, only three studies have compared return to activity following the two procedures^[1,13,49].

McCarty *et al.*^[13] reported on 75 patients who underwent either TSA ($n = 54$) or HA ($n = 21$). The authors found an 81% rate of return to sports in both the TSA group (44 of 54 patients) and the HA group (17 of 21 patients) at a minimum follow-up of two years. The authors concluded that there was no difference between TSA and HA in patients' ability to return to sports.

Zarkadas *et al.*^[1] used a mailed questionnaire to assess patient-reported activity after either TSA or HA.

Activities were classified as low-demand (*e.g.*, stationary biking and treadmill use); medium-demand (*e.g.*, fishing, dancing, and swimming); or high-demand (*e.g.*, free weights and hunting). Responses were received from 52 TSA patients and 47 HA patients. The TSA group reported better range of motion and strength than the HA group ($P < 0.05$). Sixty percent of TSA patients (27 of 52) reported having high demand use of their shoulder as compared to 46% of HA patients (11 of 47); however, this difference was not statistically significant.

Garcia *et al.*^[49] compared rates of return to sports in a matched cohort of HA and TSA patients. All arthroplasty procedures were performed for glenohumeral arthritis, and patients were followed for a minimum of two years (average 62.0 and 61.1 mo for the HA and TSA groups, respectively). The investigators found significantly higher rates of return to sport in the TSA group as compared to the HA group: Ninety-seven percent of TSA patients (36 of 37) resumed at least one sport postoperatively as compared to 65% of HA patients (19 of 29). The average time to return to full sports was similar in both groups (5.5 mo and 5.4 mo for HA and TSA patients, respectively).

To date, three studies have compared rates of return to athletic activities following HA or TSA^[1,13,49].

Only one demonstrated a difference in return to sports between the procedures, concluding that TSA was associated with more favorable rates of return to any sport as compared to HA^[49]. All of the studies are limited by their sample sizes, retrospective nature, and follow-up. The mixed results may also reflect differences in patient populations, indication for surgery, and surgeons' postoperative restrictions.

COMPARISON BETWEEN RETURN TO SPORT IN HA AND RTSA

In patients who are not candidates for anatomic TSA due to rotator cuff dysfunction, rheumatoid arthritis, or proximal humerus fracture, the choice between RTSA and HA remains controversial. As compared to HA, RTSA has been associated with improved functional and range of motion outcomes^[54-58]. However, HA is generally perceived as the "safer" option in patients who wish to remain active because there is less risk of failure^[47]. Consistent with this notion, surveys of surgeons demonstrate that they place fewer postoperative sports restrictions on HA patients than on those undergoing RTSA^[52,53]. However, limited literature exists on return to sports following RTSA and HA, and only one study to date has compared rates of return to sport following the two procedures^[47].

Liu *et al.*^[47] reported on 102 RTSA and 71 HA patients with a minimum follow-up of 1 year. All patients participated in sports preoperatively, and had a contraindication for an anatomic TSA, including rotator cuff dysfunction, inflammatory arthritis, or proximal humerus fracture. The authors found significantly higher rates of return

to sport in the RTSA group (85.9%) as compared to the HA (66.7%) group. The RTSA patients also had subjectively higher satisfaction scores regarding their surgery and their ability to return to sports. Female sex, age under 70 years, surgery on the dominant extremity, and a preoperative diagnosis of arthritis with rotator cuff dysfunction predicted a higher likelihood of return to sports for patients undergoing RTSA compared with HA. There were no significant differences in the time to return to full sports between HA (6.2 mo) and RTSA (5.3 mo). No sports-related complications occurred.

Surgeons have been shown to impose much more stringent restrictions on activities following RTSA as compared to HA^[52,53], but recent data demonstrates higher rates of return to sports following RTSA than HA^[47]. RTSA may be particularly beneficial in certain patient populations, including females, patients under 70 years old, patients with dominant shoulder pathology, and patients with a preoperative diagnosis of arthritis and rotator cuff dysfunction. The conclusions of this study should be interpreted in light of its length of follow-up (31 mo for the RTSA group and 62 mo for the HA group), lack of radiographic outcomes, and differences in the two patient populations.

SURGEONS' PREFERENCES REGARDING RETURN TO SPORTS FOLLOWING SHOULDER ARTHROPLASTY

Several studies have reported on the recommendations of experienced shoulder surgeons regarding return to sport following shoulder arthroplasty^[14,52,53,59]. Long-term outcome studies are needed to assess whether these surgeon preferences are clinically supported by patient outcomes or implant survival in patients who participate in sports after shoulder arthroplasty.

Jensen *et al.*^[14] surveyed 50 surgeons from the American Shoulder and Elbow Society (ASES) on return to golf following TSA; responses were received from 44 (88%) of the surgeons queried. Ninety-one percent of the responding surgeons allowed their patients to resume playing golf at an average of 4.3 mo. However, 29.5% of surgeons surveyed believed that participation in sports following TSA may accelerate component wear^[59].

Healy *et al.*^[60] surveyed 35 surgeons in the ASES regarding participation in 42 different athletic activities following TSA. Surgeons were instructed to rate each activity as one of the following: Recommended/allowed, allowed with experience, not recommended, and no opinion. Not surprisingly, low impact sports such as swimming, dancing, bowling, doubles tennis, and bicycling were recommended and allowed. Activities that were allowed with experience included golf, ice skating, and downhill skiing. The authors determined that only four activities of the list of forty-two were not recommended, including hockey, rock climbing, gymnastics, and football. Activities for which a consensus could not be reached

included: Baseball/softball, lacrosse, rowing, soccer, weight lifting, and singles tennis.

Magnussen *et al.*^[53] queried the members of ASES as well as the European Society for Surgery of the Shoulder and Elbow about return to sports after TSA, RTSA, or HA. The survey contained 37 activities and participants were instructed to classify their postoperative recommendations for each activity as one of the following: Allowed, allowed with experience, not allowed, or undecided. Looking specifically at TSA, almost all of the 94 responding surgeons indicated that they would allow their patients to participate in noncontact activities, such as jogging/running (86%), stationary cycling (91%), and dancing (87%). Although the majority of surgeons would also permit low impact activities following RTSA, other activity restrictions were more conservative than those following TSA or HA. For example, swimming was permitted by the majority surgeons following TSA (82%) and HA (87%), but less than half (45%) would permit participation following RTSA. Similarly, golf was allowed by most surgeons after TSA (75%) or HA (77%), but only 45% of surgeons would permit golf following RTSA; doubles tennis was allowed by about half of surgeons following TSA (48%) or HA (55%), but only permitted by 15% after RTSA. Time to return to sport following RTSA was comparable to that of TSA, with most (56%) of the responding surgeons allowing patients to resume their maximum level of activity 5-7 mo after RTSA. Twenty percent of surgeons, however, required patients to wait at least 8 mo after RTSA to return to this level of activity.

Magnussen *et al.*^[53] found that recommendations on return to sport following HA were the most lenient. For example, weight-lifting was not recommended following RTSA (82%) or TSA (57%), but permitted or allowed with experience following HA according to 52% of the surgeons surveyed.

Nearly half of surgeons (47%) would allow patients to resume their maximum level of activity earlier following HA, at 2-4 mo postoperatively. Patients were also allowed to return to sports faster following HA, with 48% of surgeons allowing return to maximum level of activity 5-7 mo postoperatively and 47% allowing return to this level earlier, at 2-4 mo postoperatively.

More recently, Golant *et al.*^[52] surveyed 310 members of the ASES regarding what types of activities they allow their patients to participate in after five different types of shoulder arthroplasty. Responses were received from 94 surgeons (30.3%). Regarding activities after TSA, 59.1% of the surgeons surveyed indicated that they allow their patients to participate in low-impact sports (including golf, bowling, rowing, and swimming) without limitations. About 20% of the surgeons surveyed would permit participation in high-impact sports (including tennis, squash, volleyball, and baseball) without limitations, and 8.2% of the surgeons reported that they would allow participation in contact sports (including football, lacrosse, hockey, and basketball) without limitations.

Consistent with the findings of Magnussen *et al.*^[53]

restrictions following RTSA were found to be the most stringent of the arthroplasty procedures evaluated. For example, 25.7% of surgeons polled by Golant *et al.*^[52] would allow their patients to participate in low-impact sports, such as golf and swimming, without restrictions, as compared to 59.1% and 80% of surgeons allowing participation following TSA and HA, respectively. Similar trends were observed with high-impact and contact sports: High-impact sports were allowed with limitations by a greater proportion of surgeons following HA (31.9%) or TSA (39.7%) than RTSA (19.4%); contact sports were allowed with limitations by about one in five surgeons following HA (21.6%) or TSA (18.5%), but only 5.2% of surgeons following RTSA.

In the available literature, there is extensive variation in surgeon recommendations on activity restrictions after joint arthroplasty. The majority of surgeons allow return to noncontact, low-load activities after all types of shoulder arthroplasty. Restrictions on high-impact sports, sports with fall risk, and contact sports were more liberal following HA or TSA as compared to RTSA.

CONCLUSION

The majority of patients are able to return to their pre-operative level of activity following TSA, RTSA, and shoulder HA. The rates of return to sports following TSA (75%-100%)^[45-46] are slightly higher than those reported for HA (67% to 76%)^[45-46] and RTSA (75%-85%)^[24,39], although this may reflect differences in patient population or surgical indication. Noncontact, low demand activities are permitted by most surgeons postoperatively and generally have higher return rates than contact sports or high-demand activities. Most patients can expect to return to sports within six months postoperatively, and many will experience an improvement in their ability to participate in sports following the arthroplasty procedure.

REFERENCES

- Zarkadas PC, Throckmorton TQ, Dahm DL, Sperling J, Schleck CD, Cofield R. Patient reported activities after shoulder replacement: total and hemiarthroplasty. *J Shoulder Elbow Surg* 2011; **20**: 273-280 [PMID: 20951063 DOI: 10.1016/j.jse.2010.06.007]
- Kim SH, Wise BL, Zhang Y, Szabo RM. Increasing incidence of shoulder arthroplasty in the United States. *J Bone Joint Surg Am* 2011; **93**: 2249-2254 [PMID: 22258770 DOI: 10.2106/JBJS.J.01994]
- Fehring EV, Kopjar B, Boorman RS, Churchill RS, Smith KL, Matsen FA. Characterizing the functional improvement after total shoulder arthroplasty for osteoarthritis. *J Bone Joint Surg Am* 2002; **84-A**: 1349-1353 [PMID: 12177264]
- Haines JF, Trail IA, Nuttall D, Birch A, Barrow A. The results of arthroplasty in osteoarthritis of the shoulder. *J Bone Joint Surg Br* 2006; **88**: 496-501 [PMID: 16567785 DOI: 10.1302/0301-620X.88.B4.16604]
- Raiss P, Schmitt M, Bruckner T, Kasten P, Pape G, Loew M, Zeifang F. Results of cemented total shoulder replacement with a minimum follow-up of ten years. *J Bone Joint Surg Am* 2012; **94**: e1711-e1710 [PMID: 23224391 DOI: 10.2106/JBJS.K.00580]
- Young A, Walch G, Boileau P, Favard L, Gohlke F, Loew M, Molé D. A multicentre study of the long-term results of using a flat-back polyethylene glenoid component in shoulder replacement for primary osteoarthritis. *J Bone Joint Surg Br* 2011; **93**: 210-216 [PMID: 21282761 DOI: 10.1302/0301-620X.93B2.25086]
- Deshmukh AV, Koris M, Zurakowski D, Thornhill TS. Total shoulder arthroplasty: long-term survivorship, functional outcome, and quality of life. *J Shoulder Elbow Surg* 2005; **14**: 471-479 [PMID: 16194737 DOI: 10.1016/j.jse.2005.02.009]
- Boileau P, Watkinson D, Hatzidakis AM, Hovorka I. Neer Award 2005: The Grammont reverse shoulder prosthesis: results in cuff tear arthritis, fracture sequelae, and revision arthroplasty. *J Shoulder Elbow Surg* 2006; **15**: 527-540 [PMID: 16979046 DOI: 10.1016/j.jse.2006.01.003]
- Handoll HH, Brorson S. Interventions for treating proximal humeral fractures in adults. *Cochrane Database Syst Rev* 2015; (11): CD000434 [PMID: 26560014 DOI: 10.1002/14651858.CD000434.pub4]
- Mulieri P, Dunning P, Klein S, Pupello D, Frankle M. Reverse shoulder arthroplasty for the treatment of irreparable rotator cuff tear without glenohumeral arthritis. *J Bone Joint Surg Am* 2010; **92**: 2544-2556 [PMID: 21048173 DOI: 10.2106/JBJS.I.00912]
- Wall B, Nové-Josserand L, O'Connor DP, Edwards TB, Walch G. Reverse total shoulder arthroplasty: a review of results according to etiology. *J Bone Joint Surg Am* 2007; **89**: 1476-1485 [PMID: 17606786]
- Khair MM, Dines JS, Dines DM. Shoulder arthroplasty: return to sport. *Sports Health* 2015; **7**: 87-89 [PMID: 25553218 DOI: 10.1177/1941738114550988]
- McCarty EC, Marx RG, Maerz D, Altchek D, Warren RF. Sports participation after shoulder replacement surgery. *Am J Sports Med* 2008; **36**: 1577-1581 [PMID: 18539951 DOI: 10.1177/0363546508317126]
- Jensen KL, Rockwood CA. Shoulder arthroplasty in recreational golfers. *J Shoulder Elbow Surg* 1998; **7**: 362-367 [PMID: 9752645 DOI: 10.1016/S1058-2746(98)90024-6]
- Schumann K, Flury MP, Schwyzer HK, Simmen BR, Drerup S, Goldhahn J. Sports activity after anatomical total shoulder arthroplasty. *Am J Sports Med* 2010; **38**: 2097-2105 [PMID: 20616374 DOI: 10.1177/0363546510371368]
- Jackson JD, Smith J, Shah JP, Wisniewski SJ, Dahm DL. Golf after total knee arthroplasty: do patients return to walking the course? *Am J Sports Med* 2009; **37**: 2201-2204 [PMID: 19684299 DOI: 10.1177/0363546509339009]
- Bradbury N, Borton D, Spoo G, Cross MJ. Participation in sports after total knee replacement. *Am J Sports Med* 1998; **26**: 530-535 [PMID: 9689373]
- Dubs L, Gschwend N, Munzinger U. Sport after total hip arthroplasty. *Arch Orthop Trauma Surg* 1983; **101**: 161-169 [PMID: 6870503 DOI: 10.1007/BF00436765]
- Gschwend N, Frei T, Morscher E, Nigg B, Loehr J. Alpine and cross-country skiing after total hip replacement: 2 cohorts of 50 patients each, one active, the other inactive in skiing, followed for 5-10 years. *Acta Orthop Scand* 2000; **71**: 243-249 [PMID: 10919294 DOI: 10.1080/000164700317411825]
- Huch K, Müller KA, Stürmer T, Brenner H, Puhl W, Günther KP. Sports activities 5 years after total knee or hip arthroplasty: the Ulm Osteoarthritis Study. *Ann Rheum Dis* 2005; **64**: 1715-1720 [PMID: 15843453 DOI: 10.1136/ard.2004.033266]
- Mallon WJ, Callaghan JJ. Total hip arthroplasty in active golfers. *J Arthroplasty* 1992; **7** Suppl: 339-346 [PMID: 1431914 DOI: 10.1016/S0883-5403(07)80022-2]
- Mallon WJ, Callaghan JJ. Total knee arthroplasty in active golfers. *J Arthroplasty* 1993; **8**: 299-306 [PMID: 8326312 DOI: 10.1016/S0883-5403(06)80093-8]
- Ries MD, Philbin EF, Groff GD, Sheesley KA, Richman JA, Lynch F. Improvement in cardiovascular fitness after total knee arthroplasty. *J Bone Joint Surg Am* 1996; **78**: 1696-1701 [PMID: 8934484]
- Garcia GH, Taylor SA, DePalma BJ, Mahony GT, Grawe BM, Nguyen J, Dines JS, Dines DM, Warren RF, Craig EV, Gulotta LV. Patient Activity Levels After Reverse Total Shoulder Arthroplasty: What Are Patients Doing? *Am J Sports Med* 2015; **43**: 2816-2821

- [PMID: 26316610 DOI: 10.1177/0363546515597673]
- 25 **Torchia ME**, Cofield RH, Settergren CR. Total shoulder arthroplasty with the Neer prosthesis: long-term results. *J Shoulder Elbow Surg* 1997; **6**: 495-505 [PMID: 9437598 DOI: 10.1016/S1058-2746(97)90081-1]
 - 26 **Montoya F**, Magosch P, Scheiderer B, Lichtenberg S, Melean P, Habermeyer P. Midterm results of a total shoulder prosthesis fixed with a cementless glenoid component. *J Shoulder Elbow Surg* 2013; **22**: 628-635 [PMID: 23107145 DOI: 10.1016/j.jse.2012.07.005]
 - 27 **Day JS**, Lau E, Ong KL, Williams GR, Ramsey ML, Kurtz SM. Prevalence and projections of total shoulder and elbow arthroplasty in the United States to 2015. *J Shoulder Elbow Surg* 2010; **19**: 1115-1120 [PMID: 20554454 DOI: 10.1016/j.jse.2010.02.009]
 - 28 **Bühlhoff M**, Sattler P, Bruckner T, Loew M, Zeifang F, Raiss P. Do patients return to sports and work after total shoulder replacement surgery? *Am J Sports Med* 2015; **43**: 423-427 [PMID: 25406301 DOI: 10.1177/0363546514557940]
 - 29 **Schmidt-Wiethoff R**, Wolf P, Lehmann M, Habermeyer P. [Physical activity after shoulder arthroplasty]. *Sportverletz Sportschaden* 2002; **16**: 26-30 [PMID: 11951162 DOI: 10.1055/s-2002-25049]
 - 30 **Vogel LA**, Carotenuto G, Basti JJ, Levine WN. Physical activity after total joint arthroplasty. *Sports Health* 2011; **3**: 441-450 [PMID: 23016041 DOI: 10.1177/1941738111415826]
 - 31 **Wierks C**, Skolasky RL, Ji JH, McFarland EG. Reverse total shoulder replacement: intraoperative and early postoperative complications. *Clin Orthop Relat Res* 2009; **467**: 225-234 [PMID: 18685908 DOI: 10.1007/s11999-008-0406-1]
 - 32 **Kempton LB**, Ankersen E, Wiater JM. A complication-based learning curve from 200 reverse shoulder arthroplasties. *Clin Orthop Relat Res* 2011; **469**: 2496-2504 [PMID: 21328021 DOI: 10.1007/s11999-011-1811-4]
 - 33 **Nam D**, Kepler CK, Neviasser AS, Jones KJ, Wright TM, Craig EV, Warren RF. Reverse total shoulder arthroplasty: current concepts, results, and component wear analysis. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 23-35 [PMID: 21189245 DOI: 10.2106/JBJS.J.00769]
 - 34 **Jain NB**, Yamaguchi K. The contribution of reverse shoulder arthroplasty to utilization of primary shoulder arthroplasty. *J Shoulder Elbow Surg* 2014; **23**: 1905-1912 [PMID: 25304043 DOI: 10.1016/j.jse.2014.06.055]
 - 35 Trends and Regional Variation in Hip, Knee and Shoulder Replacement. The Dartmouth Institute for Health Policy & Clinical Practice. 2016-02-28. Available from: URL: <http://www.dartmouthatlas.org>
 - 36 **Ponce BA**, Oladeji LO, Rogers ME, Menendez ME. Comparative analysis of anatomic and reverse total shoulder arthroplasty: in-hospital outcomes and costs. *J Shoulder Elbow Surg* 2015; **24**: 460-467 [PMID: 25441557 DOI: 10.1016/j.jse.2014.08.016]
 - 37 **Weiss JM**, Noble PC, Conditt MA, Kohl HW, Roberts S, Cook KF, Gordon MJ, Mathis KB. What functional activities are important to patients with knee replacements? *Clin Orthop Relat Res* 2002; **(404)**: 172-188 [PMID: 12439258 DOI: 10.1097/00003086-20021000-00030]
 - 38 **Wyld V**, Hewlett S, Learmonth ID, Cavendish VJ. Personal impact of disability in osteoarthritis: patient, professional and public values. *Musculoskeletal Care* 2006; **4**: 152-166 [PMID: 17042026 DOI: 10.1002/msc.86]
 - 39 **Edwards TB**, Williams MD, Labriola JE, Elkousy HA, Gartsman GM, O'Connor DP. Subscapularis insufficiency and the risk of shoulder dislocation after reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2008; **18**: 892-896 [PMID: 19282204 DOI: 10.1016/j.jse.2015.03.011]
 - 40 **Lawrence TM**, Ahmadi S, Sanchez-Sotelo J, Sperling JW, Cofield RH. Patient reported activities after reverse shoulder arthroplasty: part II. *J Shoulder Elbow Surg* 2012; **21**: 1464-1469 [PMID: 22365817 DOI: 10.1016/j.jse.2011.11.012]
 - 41 **Simovitch RW**, Gerard BK, Brees JA, Fullick R, Kearse JC. Outcomes of reverse total shoulder arthroplasty in a senior athletic population. *J Shoulder Elbow Surg* 2015; **24**: 1481-1485 [PMID: 25958214 DOI: 10.1016/j.jse.2008.12.013]
 - 42 **Wirth MA**, Tapscott RS, Southworth C, Rockwood CA. Treatment of glenohumeral arthritis with a hemiarthroplasty: a minimum five-year follow-up outcome study. *J Bone Joint Surg Am* 2006; **88**: 964-973 [PMID: 16651570 DOI: 10.2106/JBJS.D.03030]
 - 43 **Levy O**, Copeland SA. Cementless surface replacement arthroplasty (Copeland CSRA) for osteoarthritis of the shoulder. *J Shoulder Elbow Surg* 20004; **13**: 266-271 [PMID: 15111895 DOI: 10.1016/j.jse.2004.01.005]
 - 44 **Levine WN**, Fischer CR, Nguyen D, Flatow EL, Ahmad CS, Bigliani LU. Long-term follow-up of shoulder hemiarthroplasty for glenohumeral osteoarthritis. *J Bone Joint Surg Am* 2012; **94**: e164 [PMID: 23172331 DOI: 10.2106/JBJS.K.00603]
 - 45 **Garcia GH**, Mahony GT, Fabricant PD, Wu HH, Dines DM, Warren RF, Craig EV, Gulotta LV. Sports- and Work-Related Outcomes After Shoulder Hemiarthroplasty. *Am J Sports Med* 2016; **44**: 490-496 [PMID: 26657261 DOI: 10.1177/0363546515613077]
 - 46 **Skutek M**, Fremerey RW, Bosch U. Level of physical activity in elderly patients after hemiarthroplasty for three- and four-part fractures of the proximal humerus. *Arch Orthop Trauma Surg* 1998; **117**: 252-255 [PMID: 9581254 DOI: 10.1007/s004020050239]
 - 47 **Liu JN**, Garcia GH, Mahony G, Wu HH, Dines DM, Warren RF, Gulotta LV. Sports after shoulder arthroplasty: a comparative analysis of hemiarthroplasty and reverse total shoulder replacement. *J Shoulder Elbow Surg* 2016; **25**: 920-926 [PMID: 26853758 DOI: 10.1016/j.jse.2015.11.003]
 - 48 **Mann T**, Baumhauer JF, O'Keefe RJ, Harrast J, Hurwitz SR, Voloshin I. High incidence of hemiarthroplasty for shoulder osteoarthritis among recently graduated orthopaedic surgeons. *Clin Orthop Relat Res* 2014; **472**: 3510-3516 [PMID: 25146057 DOI: 10.1007/s11999-014-3823-3]
 - 49 **Garcia GH**, Liu JN, Mahony GT, Sinatro A, Wu HH, Craig EV, Warren RF, Dines DM, Gulotta LV. Hemiarthroplasty Versus Total Shoulder Arthroplasty for Shoulder Osteoarthritis: A Matched Comparison of Return to Sports. *Am J Sports Med* 2016; Epub ahead of print [PMID: 26960913 DOI: 10.1177/0363546516632527]
 - 50 **Bryant D**, Litchfield R, Sandow M, Gartsman GM, Guyatt G, Kirkley A. A comparison of pain, strength, range of motion, and functional outcomes after hemiarthroplasty and total shoulder arthroplasty in patients with osteoarthritis of the shoulder. A systematic review and meta-analysis. *J Bone Joint Surg Am* 2005; **87**: 1947-1956 [PMID: 16140808 DOI: 10.2106/JBJS.D.02854]
 - 51 **Radnay CS**, Setter KJ, Chambers L, Levine WN, Bigliani LU, Ahmad CS. Total shoulder replacement compared with humeral head replacement for the treatment of primary glenohumeral osteoarthritis: a systematic review. *J Shoulder Elbow Surg* 2007; **16**: 396-402 [PMID: 17582789 DOI: 10.1016/j.jse.2006.10.017]
 - 52 **Golant A**, Christoforou D, Zuckerman JD, Kwon YW. Return to sports after shoulder arthroplasty: a survey of surgeons' preferences. *J Shoulder Elbow Surg* 2012; **21**: 554-560 [PMID: 21393018 DOI: 10.1016/j.jse.2010.11.021]
 - 53 **Magnussen RA**, Mallon WJ, Willems WJ, Moorman CT. Long-term activity restrictions after shoulder arthroplasty: an international survey of experienced shoulder surgeons. *J Shoulder Elbow Surg* 2011; **20**: 281-289 [PMID: 21051242 DOI: 10.1016/j.jse.2010.07.021]
 - 54 **Alentorn-Geli E**, Guirro P, Santana F, Torrens C. Treatment of fracture sequelae of the proximal humerus: comparison of hemiarthroplasty and reverse total shoulder arthroplasty. *Arch Orthop Trauma Surg* 2014; **134**: 1545-1550 [PMID: 25138037 DOI: 10.1007/s00402-014-2074-9]
 - 55 **Boyle MJ**, Youn SM, Frampton CM, Ball CM. Functional outcomes of reverse shoulder arthroplasty compared with hemiarthroplasty for acute proximal humeral fractures. *J Shoulder Elbow Surg* 2013; **22**: 32-37 [PMID: 22652065 DOI: 10.1016/j.jse.2012.03.006]
 - 56 **Ferrel JR**, Trinh TQ, Fischer RA. Reverse total shoulder arthroplasty versus hemiarthroplasty for proximal humeral fractures: a systematic review. *J Orthop Trauma* 2015; **29**: 60-68 [PMID: 25186842 DOI: 10.1097/BOT.0000000000000224]
 - 57 **Leung B**, Horodyski M, Struk AM, Wright TW. Functional outcome of hemiarthroplasty compared with reverse total shoulder arthroplasty in the treatment of rotator cuff tear arthropathy. *J*

Shoulder Elbow Surg 2012; **21**: 319-323 [PMID: 21872496 DOI: 10.1016/j.jse.2011.05.023]

- 58 **Young SW**, Zhu M, Walker CG, Poon PC. Comparison of functional outcomes of reverse shoulder arthroplasty with those of hemiarthroplasty in the treatment of cuff-tear arthropathy: a matched-pair analysis. *J Bone Joint Surg Am* 2013; **95**: 910-915

[PMID: 23677358 DOI: 10.2106/JBJS.L.00302]

- 59 **Clifford PE**, Mallon WJ. Sports after total joint replacement. *Clin Sports Med* 2005; **24**: 175-186 [PMID: 15636785 DOI: 10.1016/j.csm.2004.08.009]

- 60 **Healy WL**, Iorio R, Lemos MJ. Athletic activity after joint replacement. *Am J Sports Med* 2001; **29**: 377-388 [PMID: 11394613]

P- Reviewer: Anand A, Hasegawa M
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D



Management of Ewing sarcoma family of tumors: Current scenario and unmet need

Bivas Biswas, Sameer Bakhshi

Bivas Biswas, Sameer Bakhshi, Department of Medical Oncology, Dr.B.R.A.I.R.C.H, All India Institute of Medical Sciences, New Delhi 110029, India

Author contributions: Biswas B performed the literature search, critical analysis, wrote the paper recorded the audio core tip; Bakhshi S reviewed and edited the paper and done the critical analysis.

Conflict-of-interest statement: No potential conflicts of interest to declare for each author.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Bivas Biswas, Assistant Professor, Department of Medical Oncology, Dr.B.R.A.I.R.C.H, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India. bivasbiswas@gmail.com
Telephone: +91-98-30922005
Fax: +91-11-26588663

Received: April 27, 2016
Peer-review started: April 28, 2016
First decision: June 16, 2016
Revised: June 21, 2016
Accepted: July 11, 2016
Article in press: July 13, 2016
Published online: September 18, 2016

Abstract

Ewing sarcoma family tumors (ESFT) are heterogeneous, aggressive group of disease with peak in-

cidence in adolescent and young adults. The outcome has been improved dramatically from 10% with surgery and radiotherapy alone to 65%-70% now, in localized disease, with the introduction of chemotherapy. Chemotherapy regimen evolved from single agent to multiagent with effort of many cooperative clinical trials over decades. The usual treatment protocol include introduction of multi-agent chemotherapy in neoadjuvant setting to eradicate systemic disease with timely incorporation of surgery and/or radiotherapy as local treatment modality and further adjuvant chemotherapy to prevent recurrence. Risk adapted chemotherapy in neoadjuvant and adjuvant setting along with radiotherapy has been used in many international collaborative trials and has resulted in improved outcome, more so in patients with localized disease. The role of high dose chemotherapy with stem cell rescue is still debatable. The outcome of patients with metastatic disease is dismal with long term outcome ranges from 20%-40% depending on the sites of metastasis and intensity of treatment. There is a huge unmet need to improve outcome further, more so in metastatic setting. Novel therapy targeting the molecular pathways and pathogenesis of ESFT is very much required. Here we have discussed the current standard of management in patients with ESFT, investigational targeted or novel therapies along with future promises.

Key words: Outcome; Review; Chemotherapy; Ewing sarcoma; Targeted therapy; Radiotherapy; Prognostic factors

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Ewing sarcoma family tumors are a heterogeneous and aggressive group of disease of bone and soft tissue in childhood. The outcome has improved with introduction of chemotherapy and multimodality management. But, the prognosis of patients with metastatic disease is dismal. Novel targeted therapies

are investigational and may offer some hope in future, especially in metastatic setting. In this review we have discussed current treatment modality, prognostic factors, ongoing trials and novel investigational therapies.

Biswas B, Bakhshi S. Management of Ewing sarcoma family of tumors: Current scenario and unmet need. *World J Orthop* 2016; 7(9): 527-538 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/527.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.527>

INTRODUCTION

Ewing sarcoma families of tumors (ESFT) are a heterogeneous and aggressive group of disease of bone and soft tissue that includes classical Ewing sarcoma, peripheral primitive neuroectodermal tumor and Askin tumor. It is the 2nd most common primary malignant bone tumor (34%) after osteosarcoma^[1] with peak in 2nd decade of life, though approximately 20% to 30% of all cases occur in 1st decade. Over the last four decades, the survival has been improved from 10% with radiotherapy alone to near 70%, in localized disease, with the introduction of chemotherapy and multimodality approach. This improvement in outcome has been achieved after many international collaborative clinical trials and close liaison between orthopedic surgeons, adult and pediatric oncologists, radiation oncologist, pediatric surgeons, biomedical engineers, pathologists and radiologists as well as invention of better diagnostic imaging, radiotherapy techniques and prosthesis.

With the improvement in outcome and more number of long-term survivors, the focus is now on to minimize toxicities, such as chemotherapy related, radiotherapy related and surgery related long-term complication without compromising the oncological outcomes. The multidisciplinary approach with risk adapted chemotherapy and local treatment (surgery and/or radiotherapy) has been used in recent times in many collaborative trials to minimize the overtreatment and thus treatment related side effects with maintaining high cure rates. This approach is the current standard of care in maximum institutions all over the globe.

Even with current armamentarium the outcome of ESFT patients with metastatic disease is dismal with cure rate varying between 20%-40%^[2,3] and even less in those with recurrent/refractory diseases. The current emphasis is to improve the survival outcome in ESFT patients with metastatic disease and also in the recurrent setting. There is a vacuum in novel and targeted therapies as compared to adult solid tumors, and there lies a huge unmet need to improve the outcome of poor risk ESFTs.

Researchers across the world have tried to understand the pathogenesis of ESFT along with the molecular downstream pathways enhancing the survival of ESFT tumor cells. The primary focus was on *EWS-FLI1* fusion

oncogene, and other similar fusions that were thought to drive the oncogenic pathway in ESFT, but targeted therapy by blocking its product has not resulted into any meaningful clinical outcome^[4,5]. In this review we have discussed the current standard of treatment-chemotherapy, local treatment modalities, role of high dose chemotherapy, and salvage treatment along with novel targeted therapies under investigation and potential future promises.

WHAT ARE THE CLINICALLY RELEVANT PROGNOSTIC FACTORS?

Many international cooperative trials has been performed over last four decades to improve the outcome of ESFTs and further analysis of those studies revealed many prognostic factors that predicted differential outcomes and successively helped in designing tailored clinical trials to optimize the treatment strategies depending on the risk group and to decrease over treatment and treatment related side effects. Further refinements and validation of those prognostic factors (clinic-pathological and treatment related factors) has been done in further studies and in routine clinical practices. Amongst all the clinic-pathological and treatment related factors, presence of metastasis at baseline is the strongest prognostic factor and has been proven in all clinical studies and routine clinical practices. The prognosis also depends on burden of metastasis and site of metastasis. Spectrum of outcome varies from worst with bone marrow metastasis (3-year EFS of < 10%) with non-pulmonary metastasis in the middle and single pulmonary metastasis having the best outcome (3-year EFS of 40%-50%)^[6-10]. No research group or study had prospectively evaluated the prognostic significance of burden of metastasis until recently. Study from our center in ESFT patients with metastatic disease found hypoalbuminemia (< 3.5 g/dL) as a novel and independent poor prognostic factor to affect outcome^[2]. The recent EuroEwing 99 (EE99) systematically risk stratified the metastatic group and the 3rd randomized arm (disseminated multifocal ESFT) identified novel prognostic factors, such as - age at diagnosis > 14 years, presence and number of bone metastasis, number of pulmonary metastasis and bone marrow involvement and also developed a prognostic score to predict differential outcome ranging from 8%-40%^[10].

Systemic symptom (fever and weight loss) is a poor prognostic factor along with high lactate dehydrogenase level that denotes tumor burden. These two prognostic factors has been used to risk stratify ESFT patients to tailor therapy. Tumor size and tumor volume is well established prognostic across the clinical studies with tumor size > 8 cm^[11] and tumor volume > 200 mL^[12,13] is poor prognostic and has been used in all clinical trials for risk adapted therapies. Site of primary tumor is also of prognostic significance with axial primary especially pelvic location is poor prognostic. Both tumor size and pelvic primary has been proven as poor prognostic in

our institutional experience^[2,14]. But recently histological response to neoadjuvant chemotherapy (poor response has been defined as > 10% viable tumor cells as per Salzer-Kuntschik grading system^[13]) has been emerged as the strongest prognostic factor overriding tumor size, tumor volume or tumor location. The recent EE99 study risk stratified ESFT patients in respect to histological response to chemotherapy to tailor therapy^[15]. WBC count has been emerged as independent prognostic factor in our experience of ESFT^[14,16-18] treated with uniform chemotherapy protocol with high WBC (> 11000/ μ L) having poor outcome. It may signify micrometastatic disease and inflammatory nature of the disease and will require further validation in a prospective study.

Collaborative efforts have been made to identify potential biomarker in this rare aggressive tumor. Early retrospective studies^[19,20] reported prognostic significance of different transcripts (*EWS-ETS* fusion types) but failed to do so in prospective studies^[21]. High throughput methods has revealed gene copy number variations^[22], such as - 1q-, 18q-, 20-, 16q+ along with mutation in *TP53*, *CDKN2A* and *STAT2* and concurrent presence of *STAT2* and *TP53* reported as poor prognostic^[23]. Detection of disseminated tumor cells in blood and bone marrow^[24] in localized patients (up to 20%) found to poor prognostic and its detection after completion of therapy (minimal residual disease) by flow cytometry or other sensitive method can tailor therapy, detect early recurrence and can be of future prognostic significance^[20].

WHAT IS THE ROLE OF BIO-IMAGING?

Histological response to neoadjuvant chemotherapy is the strongest prognostic factor in localized ESFT and metastatic disease is the strongest one in whole cohort of ESFT. Efforts have been made to predict metastatic potential of ESFT in view of its aggressive nature and to escalate therapy in case of poor responder before initiation of local therapy. 18F-FDG PET is a relatively non-invasive test that can escape invasive diagnostic metastatic work-up like bone marrow aspiration/biopsy and tissue diagnosis in case of doubtful lung metastasis if it predicts site of metastases, and also post chemotherapy response assessment before the histological response is assessed. Retrospective studies have shown it can predict response to neoadjuvant chemotherapy and have a high concordance rate with the histological response by measuring reduction in standardized uptake value^[25,26] and also reduction in metabolic tumor volume^[27]. But no prospective study has been done in regards to its predicting power of detecting metastasis and to predict response to chemotherapy before its utilization in routine clinical practice.

LOCALIZED DISEASE

What chemotherapy, what intensity, and how long?

Historically, in early 1970s the outcome of ESFT with

radiotherapy and surgery alone was dismal with only < 10% patients surviving and all invariably experienced relapse within 2 years. With the introduction of chemotherapy the outcome have improved drastically to 70% cure rate in localized disease. The evolution of chemotherapy started from single agent vincristine to multiagent chemotherapy (VAC - vincristine, actinomycin D and cyclophosphamide) and from adjuvant to neoadjuvant setting (Table 1). Then comes the role of anthracyclines and addition of doxorubicin resulted in improved survival in 342 localized ESFT along with additional benefit of whole lung irradiation (WLI) in metastasis prevention in Intergroup Ewing's Sarcoma Study 1 (IESS-1)^[28]. The value of doxorubicin further potentiated in IESS- II which showed that high dose intermittent doxorubicin is better than low dose continuous therapy in 214 non-pelvic localized ESFT^[29]. The landmark United States intergroup study (INT0091) by Grier *et al*^[6] showed additional benefit of ifosfamide and etoposide (IE) in addition to vincristine, doxorubicin, cyclophosphamide (VDC) in localized patients with ESFT after the beneficial effect of IE has been demonstrated in recurrent setting^[30], but the trial failed to demonstrate any benefit of IE in a relatively smaller numbers of patients with metastatic disease. Replacement of ifosfamide with cyclophosphamide has showed conflicting results^[31] and EICESS-92 trial showed similar result with four drug chemotherapy regimen in a relatively underpowered study of 155 localized ESFT along with non-significant advantage of addition of etoposide in metastatic disease^[7]. In a different strategy to improve outcome by intensifying the alkylator dose and thus reducing the chemotherapy duration to 30 wk as compared to standard 48 wk with VDC-IE failed to improve outcomes in a United States intergroup trial (INT 154)^[32]. But subsequent Children Oncology Group (COG) study used dose compressed study of 3-weekly vs 2-weekly VDC-IE with use of filgrastim, thus maintaining the dose intensity, and demonstrated superior outcome in 2-weekly arm (5-year EFS of 73% vs 65%, $P = 0.048$)^[33] without any increasing toxicity in the experimental arm. The latest and largest trial in ESFT is the ongoing EE99 trial that compared cyclophosphamide with ifosfamide in standard risk ESFT and the early result showed equivalent outcome in both arm with pending long-term toxicity results^[15] (Table 2). The role of high dose chemotherapy with autologous stem cell rescue not well studied in localized disease as consolidation in comparison to continuation or maintenance chemotherapy. Two cooperative trials^[34,35] used BuMel conditioning regimen with stem cell rescue as consolidation therapy in a non-randomized manner in high risk localized disease (defined as poor histologic response to chemotherapy) and showed improved survival as compared to historical control and similar to that of standard risk patients. Following that result the recent ongoing EE99 trial randomized (arm 2) BuMel based high dose chemotherapy vs continuation of standard chemotherapy after VIDE induction chemotherapy in high risk localized patients and the result is still pending (Table 2).

Table 1 Randomized studies of chemotherapy in upfront treatment of Ewing sarcoma family tumors

Study	Patients (n)	Intervention ¹	Outcome	P	Comments
IESS I ^[78]	Localized (342)	(1) VAC (2) VACD (3) VAC + Lung RT	5-yr RFS 24% 60% 44%	–	Beneficial of doxorubicin and benefit of lung RT
IESS II ^[29]	Non-pelvic, localized (214)	VACD (1) Intermittent, high dose (3 weekly) (2) Continuous, moderate dose (weekly)	5-yr RFS 73% 56%	0.04	Intermittent, high dose better
POG-CCSG INT-0091 ^[6]	Localized (398)	(1) VDC (2) VDC + IE	5-yr RFS 54% 69%	0.005	IE is beneficial in addition to VDC in localized but not in metastatic disease
	Metastatic (120)	(1) VDC (2) VDC + IE	22% 22%	NS	
POG-CCSG INT-154 ^[32]	Localized (478)	(1) VDC + IE (standard) (2) VDC + IE (intensified)	5-yr EFS 70% 72%	NS	Dose intensification not effective
COG AEWS0031 ^[33]	Localized (568)	(1) VDC + IE (3 weekly) (2) VDC + IE (2 weekly)	5-yr EFS 65% 73%	0.05	3-weekly better than 2-weekly with no increase in toxicity
EICESS92 ^[7]	n = 155	SR (localized and < 100 mL)	3-yr EFS	NS	Cyclophosphamide and ifosfamide is similar in efficacy in SR patients
	n = 492	4#VAIA → 8#VAIA vs 8#VACD HR (metastatic, > 100 mL) 14#VAIA vs 14#EVAIA	73% vs 74% 47% vs 52%	0.12	No benefit of etoposide in HR patients
Euro-Ewing 99 ^[49]	Detailed in Table 2				

¹All chemotherapy regimens mentioned in the table is used in neoadjuvant setting followed-by local therapy (in terms of surgery and/or radiotherapy) followed by further adjuvant chemotherapy. EFS: Event free survival; EVAIA: Etoposide, vincristine, dactinomycin, ifosfamide, doxorubicin; HR: High risk; IE: Ifosfamide, etoposide; NS: Not significant; RFS: Relapse free survival; RT: Radiotherapy; SR: Standard risk; VAC: Vincristine, dactinomycin, cyclophosphamide; VACD: Vincristine, dactinomycin, cyclophosphamide, doxorubicin; VAIA: Vincristine, dactinomycin, ifosfamide, doxorubicin; VDC: Vincristine, doxorubicin, cyclophosphamide.

Table 2 Euro-Ewing 99 trial design and details

Randomized arm	Patients	n	Randomization	3-yr EFS
Arm 1	SR, Localized (good histologic response, < 200 mL + RT)	856	6#VIDE + 1#VAI f/b 7#VAI vs 7#VAC	78% vs 75%
Arm 2	HR, Localized (poor histologic response, ≥ 200 mL and RT alone) Lung metastasis only	---	6#VIDE + 1#VAI f/b 7#VAI vs BuMel (n = 281)	45% (BuMel)
Arm 3	Extrapulmonary metastasis	---	6#VIDE + 1#VAI f/b 7#VAI + WLI vs BuMel BuMel/TreoMel vs clinical trial	---

BuMel: Busulphan and melphalan; EFS: Event free survival; f/b: Followed-by; HR: High risk; n: Number; RT: Radiotherapy; SR: Standard risk; TreoMel: TresoMelfalan and melphalan; VAC: Vincristine, dactinomycin, cyclophosphamide; VAI: Vincristine, dactinomycin, ifosfamide; VIDE: Vincristine, ifosfamide, doxorubicin, etoposide; WLI: Whole lung irradiation.

What local therapy and when?

The outcome of ESFT with surgery or radiotherapy alone was dismal and with introduction of polychemotherapy regimen improved the outcome dramatically by eradicating systemic micrometastasis in localized disease. But, chemotherapy alone can't eradicate ESF tumor cells and timely incorporation of local therapy either surgery and/or radiotherapy is crucial for optimum management and to produce high cure rate. The approach of local therapy evolved over time with better understanding of the disease biology, better radiation technique, invention of newer engineered prosthesis, better imaging modalities and more information of therapy related complications. The choice of local treatment influenced by multiple factors,

such as age of the patients, site and size of the tumor, local extent of the tumor, clinic-radiological response to chemotherapy, expertise and experience of the treating institution and surgeon and patient's choice, etc. The different modalities of local treatment include - surgery (amputation, limb salvage or organ sparing surgery) with or without adjuvant radiotherapy, radical radiotherapy, pre-operative radiotherapy, extracorporeal radiotherapy. No prospective formal comparison done between surgery and radiotherapy as local treatment. Across the clinical trials and institutional experience, surgery done better in terms of long term outcome (both local and systemic control), and thus a formal comparison between this two seems not feasible in future.

ESFT is a radiosensitive tumor, but the long term outcome was < 10% with high incidence of local^[36] and systemic recurrence. Surgery slowly replaced radiotherapy in view of better local control rate, lesser long-term complication compared to radiotherapy and with invention of better bone replacement materials (endoprosthesis, bone cement, allograft, vascularized autograft) the rate of limb sparing surgery has increased as a norm now-a-days^[36,37]. But, the surgery is also associated with long-term complications, such as post-op infection, limb-length discrepancy, fractures, etc. Maintaining limb length is difficult in growing children and expandable endoprosthesis comes handy in this scenario with its increasing uses.

The surgical resection principle depends on the respectability, size and sites the tumor and its operability after chemotherapy. A functional limb or organ is the norm after any local treatment modality. Amputation is rarely indicated and limb salvage or organ sparing surgery should be tried whenever feasible. Surgical resection should be tried whenever a marginal or wide resection is feasible as the outcome seems to be superior to radical radiotherapy as local control^[11,32,36,38-42]. Intralesional or debulking surgery should be avoided as the outcome is not superior over radiotherapy alone^[41].

Definitive or radical radiotherapy as local treatment modality used where non-mutilating, wide local excision is not feasible with a functional organ, more so in axial primary, such as - head and area, spine, pelvic primary and in very large lesion not amenable to curative surgery even after neoadjuvant chemotherapy, and in case of a metastatic disease, etc. The recommended dose varies from 55 to 60 Gy in standard fractionation with 2 cm margin that should include original biopsy scar^[39]. Care should be taken to avoid toxicity to adjacent normal organ and newer techniques, such as - intensity modulated radiotherapy, image guided planning or proton therapy, etc. should be used in more cases^[40]. Data on use of post-operative radiotherapy is mostly debated in view of conflicting results from observational studies^[41-43]. The only clear cut indication is that of intralesional surgery^[32] where further resection with remaining functional organ is not feasible. Many European institutions use adjuvant radiotherapy in patients with poor histologic response to chemotherapy (> 10% viable tumor cells) and in a soft tissue primary. Recent EE99 study also showed beneficial effect of adjuvant radiotherapy even in good responder and thus broadens its future use, though the risk-benefit ratio to be calculated stringently with long-term radiotherapy related complication. Pre-operative radiation therapy is a good viable future alternative where a complete resection looks not feasible after chemotherapy and thus can sterilize the compartment before reconsideration of surgery after radiotherapy, like in pelvic or spinal primary^[40].

What are the current and future studies?

Many collaborative studies are ongoing in ESFT to find out the most appropriate risk-stratified approach for

improving outcome with incorporation of high dose chemotherapy (Ewing 2008 and Italian ISG/AIEOP EW-1 study), introduction of metronomic chemotherapy as maintenance (COG AEWS1031 study), role of zoledronic acid (Ewing 2008 and Euro-Ewing 2012 study), optimum use of post-operative radiotherapy along with dose intensified approach (Euro-Ewing 2012 study), and comparison of vincristine, ifosfamide, doxorubicin and etoposide (VIDE) standard therapy in Europe vs VAC-IE (Euro-Ewing 2012 study).

METASTATIC DISEASE

Is site of metastasis prognostic?

ESFTs are an aggressive group of disease with high incidence of metastasis at presentation ranging from 20%-40% across different clinical trials and observation studies^[2,3,44-47]. Outcome of patients with lung metastasis was better as compared to those with bone metastasis or combined or to those with bone marrow involvement and single metastasis done better as compared to multiple metastases^[7]. The recent EE99 trial also revealed the presence and number of bone metastasis, presence and number of lung metastasis and bone marrow involvement as prognostic factors^[10]. More prospective studies are needed to define the prognostic nature of site and number of metastasis in a more stringent manner to tailor and intensify therapies.

Is the treatment same as localized disease?

The treatment protocol is similar like in those with localized disease with curative intent - neoadjuvant chemotherapy followed by institution of local therapy (surgery and/or radiotherapy) and further maintenance therapy or consolidation with high dose chemotherapy or an investigation novel agents/targeted therapy. Many agents in combination or with total body irradiation have been used as consolidation in metastatic disease. Definitive radiotherapy used more as compared to surgery in view of high residual disease at metastatic disease after neoadjuvant chemotherapy and a more conservative approach especially in those with disseminated metastases or with bone marrow involvement.

LOCAL TREATMENT: WHAT AND WHEN?

Local treatment usually incorporated after initial 5-6 cycles of chemotherapy and if there is good response to chemotherapy in both local site and metastatic site(s). WLI has been tried in clinical studies in patients with lung only metastasis^[48] with 5-year EFS up to 50% along with conventional chemotherapy compared to similar results with high dose chemotherapy without WLI^[8]. The EE99 study randomized (arm 2) patients with lung only metastasis VIDE chemotherapy followed by VAI as maintenance plus WLI vs BuMel based high dose chemotherapy as consolidation and the result is

pending^[49]. Local excision or radiation therapy has been tried in patients with bone metastases in retrospective studies with favorable outcome^[50]. Resection of pulmonary metastasis failed to show efficacy in two retrospective studies^[51,52] but require validation in a prospective manner especially in those with single lung metastasis.

WHAT IS THE ROLE OF HIGH DOSE CHEMOTHERAPY?

Dose intensity^[33] and high dose chemotherapy^[34,35] found to be effective and improved outcome in patients with localized disease especially in high risk disease. With the principle of dose intensity and dose density high dose chemotherapy with stem cell rescue has been tried in many randomized and non-randomized study to improve outcome in metastatic disease with mixed results. Single agent high dose melphalan failed to improve outcome^[53]. In a single arm study, BuMel conditioning in metastatic patients showed 5-year EFS of 52% in patients with lung metastasis and 36% in those with bone metastases^[8]. Subsequently many clinical trials have tried high dose chemotherapy in metastatic patients and showed mixed outcome as compared to conventional chemotherapy only (Table 3). Three large studies using high dose chemotherapy - the EE99 study randomized lung only metastatic group in to BuMel based high dose therapy vs WLI along with conventional chemotherapy after initial VIDE chemotherapy and the mature result is pending^[49]. The third arm randomized patients with extrapulmonary metastasis in BuMel or TreoMel based high dose chemotherapy vs investigational agent after standard VIDE based induction chemotherapy regimen and the early results showed 3-year overall survival^[10]. In study by Italian and Scandinavian sarcoma study group used BuMel conditioning with WLI in patients with lung only metastasis or single bone metastasis with 5-year EFS of 43%^[9]. The Ewing 2008 trial randomized patients with extrapulmonary metastasis after VAC chemotherapy to TreoMel based high dose chemotherapy vs continuation of VAC and the result is pending. On the contrary a study by Children's Cancer Group failed to show any improvement in outcome of patients with extrapulmonary metastases after VAC-IE based chemotherapy followed by high dose chemotherapy with melphalan, etoposide and total body irradiation^[54].

RELAPSED AND RECURRENT DISEASE

The progress of improved outcome in ESFT is attenuated by high incidence of recurrence (local and/or systemic) and remains the main challenge in multidisciplinary management of this aggressive malignancy, especially in those with metastatic disease. The incidence of local or distant relapse is approximately 20%-25% in the published literature^[45,55] and can reach up to 40% in metastatic setting^[2,47]. There is no standard established salvage therapy exist in recurrent disease with dismal

outcome of 20% in case of localized relapse^[56]. Few chemotherapy agents showed activity in recurrent disease with moderate but short lasting response rate - topotecan and cyclophosphamide^[57], ifosfamide in combination with carboplatin and etoposide^[58], irinotecan and temozolamide^[59]. Gemcitabine and docetaxel^[60] combination failed to show any clinically meaningful activity in recurrent ESFT. The mostly studied chemotherapeutic regimen in recurrent ESFT is of irinotecan and temozolamide from a phase 1 trial and from few institutional experiences^[61-65], like in other pediatric solid tumors. This combination used protracted course of irinotecan with synergistic activity of temozolamide and produced overall response rate of 25%-60% (Table 4). No prospective study to evaluate role of high dose chemotherapy has been done so far in recurrent ESFT and retrospective institutional data^[66,67] is available with modest activity. A well selected prospective trial in needed in this regards. The Euro-Ewing consortium started a randomized phase II/III four arm study (cyclophosphamide-topotecan vs gemcitabine-docetaxel vs high dose ifosfamide vs irinotecan-temozolamide) in recurrent ESFT and the trial will complete recruitment in 2019. A huge vacuum exist in effective salvage therapy of recurrent/refractory ESFT and novel targeted therapy is very much need to fill that unmet need. Future therapeutic trials will eye on combination of chemotherapy with targeted therapy in recurrent/refractory as well as metastatic disease.

NEW TARGETS AND TARGETED THERAPIES

With the plateau of survival with the current conventional chemotherapy and stem cell transplantation in metastatic and recurrent setting of ESFT the urgent need for novel targeted therapy should match the ongoing research in understanding the biology of ESFT with revelation of more and more oncologic pathways and targets. Various drugs has been discovered and tested in preclinical and clinical studies in ESFT by targeting EWS-FLI1 fusion protein, the hall mark of ESFT-CD99, angiogenic pathways (VEGF and its receptor), mammalian target of rapamycin (mTOR) and insulin-like growth factor-1 (IGF1) pathways, the osteoclastic-osteoblastic homeostasis and bone microenvironment, enzymatic pathways (poly ADP-ribose polymerase 1 - PARP1), and GD2 ganglioside pathways.

The mostly studied targeted therapy used in ESFT is by inhibiting EWS-FLI1 transcriptional complex. Many agents have been discovered that directly or indirectly inhibit EWS-FLI1 pathways - small-molecule YK-4-279 is in pre-clinical phase that directly inhibit interaction of EWS-FLI1 and RNA helicase A^[68], certain chemotherapy agents (doxorubicin, etoposide and cytarabine), midostaurin (broad spectrum protein kinase inhibitor)^[69], mithramycin (antibiotic inhibiting RNA synthesis)^[70], and the early clinical studies failed to show any clinical benefit of inhibiting EWS-FLI1 pathway in spite of being the

Table 3 Selected studies of high dose chemotherapy with stem cell rescue in Ewing sarcoma family tumors

Study (type)	Disease setting	n	Conditioning	Conclusion
CESS (retrospective) ^[78]	Recurrent or progressive disease (HDC after CR or PR)	73	BuMel (15) TreoMel (38) Other (20)	Early relapse - poor prognostic
Société Française des Cancers de l'Enfant (prospective) ^[8]	Metastatic at diagnosis	75	BuMel	Beneficial for lung only or bone metastases
Italian Sarcoma Group/Scandinavian Sarcoma Group IV Protocol (phase II) ^[9]	Metastatic at diagnosis (lung or single bone metastasis)	79	BuMel ± TBI	HDC with WLI is effective
Italian Sarcoma Group/Scandinavian Sarcoma Group III Protocol (prospective) ^[34]	High risk, localized	126	BuMel	Effective and feasible in patients with PR after chemotherapy
Euro-Ewing 99 (prospective) ^[10]	Metastatic at diagnosis	169	BuMel (123) Mel (15) Others (20)	Effective in Bone and Bone marrow metastases
EBMT registry (retrospective) ^[79]	Metastatic and HR, localized (n = 2411) Recurrent (n = 719)	3695	Heterogeneous regimens	Prognostic factors: Age, response to treatment, BuMel regimen

BuMel: Busulphan and melphalan; CR: Complete response; ESFT: Ewing sarcoma family of tumors; HDC: High dose chemotherapy; HR: High risk; n: Number; PR: Partial response; TBI: Total body irradiation; TreoMel: Treosulphan and melphalan; WLI: Whole lung irradiation.

Table 4 Data on Irinotecan-temozolamide salvage regimen in recurrent/refractory Ewing sarcoma family tumors

Ref.	n	Irinotecan schedule	ORR (n)	Toxicity (grade 3 and 4)
Kurucu <i>et al</i> ^[65]	20	20 mg/m ² (D1-5 and D8-D12)	55% (11)	Diarrhea - 9.2% Neutropenia - 11.3%
McNall-Knapp <i>et al</i> ^[64]	25	15 mg/m ² vs 20 mg/m ² (D1-5 and D8-D12) ¹	20% (5)	Diarrhea - 5%
Raciborska <i>et al</i> ^[63]	22	50 mg/m ² (D1-D5) ¹	50% (12)	Diarrhea - 15% Hematological - 10%
Wagner <i>et al</i> ^[62]	16	10-20 mg/m ² (D1-5 and D8-D12) - 3 weekly vs 4 weekly	25% (4)	Diarrhea - 11%
Casey <i>et al</i> ^[61]	20	20 mg/m ² (D1-5 and D8-D12)	63%	Diarrhea - 4.5% Hematological - 22%

¹With vincristine. ESFT: Ewing sarcoma family of tumors; n: Number; ORR: Overall response rate.

driver in ESFT carcinogenesis.

Anti-angiogenic approach has been used in recurrent tumors and thus inhibiting the tumor growth and its metastatic potential. Bevacizumab (monoclonal antibody against VEGFR) has been tested in phase II study by COG in combination with chemotherapy (vincristine, topotecan and cyclophosphamide) in recurrent setting with pending results (NCT00516295). Pazopanib (a small molecule multi-kinase inhibitor including VEGFR) has been tested in a phase I trial^[71] in refractory pediatric solid tumor and now being tested in a phase II study by COG that include ESFT and other sarcomas (NCT01956669). Regorafenib (a small molecule multi-kinase inhibitor like pazopanib) also being tested in refractory sarcomas including ESFT (NCT02048371).

ESFT is characterized by osteolytic bone lesion with extensive soft tissue component which is marked by osteoclastic activity and interaction between RANK and its ligand - RANKL^[72]. RANKL facilitates osteoclastic activity, with bone resorption and destruction, and tumor growth. Zoledronic acid, a bisphosphonate inhibit osteoclastic activity and its migration along with inhibition of RANK,

showed anti-tumor activity in *in-vivo* model of ESFT and the effect was accentuated by addition of ifosfamide^[73]. Ewing 2008 and Euro-Ewing 2012 trial is evaluating the benefit of zoledronic after combining with chemotherapy in localized ESFT.

IGF1 receptor (IGF1R) plays an important role downstream to EWS-FLI1 for cell survival, angiogenesis and metastasis. But, disappointing results with anti-IGF1R monoclonal antibody led to stoppage of further study of this novel agent due to dramatic but very short lasting response in refractory ESFTs. The cause of this early resistance is not fully understood though up-regulation of IGF1R or mTOR has been postulated^[74]. The COG future trial has planned combination of VAC-IE with anti-IGF1R antibody in metastatic disease to overcome this resistance.

The other potential targeted therapies include - PARP1 inhibitor olaparib in combination with temozolamide showed *in-vivo* and *in-vitro* activity^[75], anti-GD2 ganglioside (a neuroendocrine marker present in ESFT cells) chimeric antigen^[76], and anti-CD99 monoclonal antibody^[77] are in preclinical study periods.

FERTILITY ISSUE: A IMPORTANT BUT OFTEN IGNORED ISSUE

ESFT is a disease of young adolescent age group along with many patients in reproductive age group. All three treatment modality in ESFT affects gonadal and reproductive function in these patients. Multi-agent chemotherapy, especially with alkylators and anthracyclines, and radiotherapy are the two major culprits in this scenario due to their gonadotoxic effects. Many strategies have been taken to minimize or counter the gonadotoxic effects of cancer treatment especially with chemotherapy and radiotherapy.

Sperm cryopreservation is the standard and effective modality of fertility preservation in case of male patients, whenever indicated. Toxicity to ovarian follicle and embryo is a special scenario especially with pelvic radiotherapy. In a COG study^[78], 8.3% of female cancer survivors experienced acute ovarian failure, defined as loss of ovarian function with 5-years of cancer diagnosis. Radiotherapy toxicity to ovary depends on age of the patients, concurrent ovariotoxic chemotherapy, dose and fractionation of radiotherapy and volume of radiation field. Cost, experience, expertise, infrastructure and low success rate are the main logistic issue in female fertility preservation.

Embryo cryopreservation is an option for fertility preservation in female patients with a male partner, whereas cryopreservation of mature or immature oocytes is a viable option for those refuse to opt for a sperm donor. Cumulative pregnancy rate up to 40% has been reported with the former technique^[79] but with a modest success with the later technique^[80]. Cryopreservation of ovarian tissue is the only measures of fertility preservation in very young girls, and recent reports of successful pregnancy have been described in literature^[81,82].

Ovarian transposition or ovariopexy is the method to preserve ovarian function in patients receiving pelvic radiotherapy but high rate of permanent cessation of ovarian function has been reported in earlier series^[83]. Intensity modulated radiotherapy or 3-D conformal CT planning in radiotherapy can minimize the gonadal toxicity in case of very small pelvic tumor or a tumor distant to ovary.

Protective role of concurrent GnRH-a has been described in literature during combination gonadotoxic chemotherapy. In study of lymphoma patients aged 15-40 years, GnRH-a group resumed menstruation in 93.7% cases within 3-8 mo of chemotherapy as compared to 39% in historical controls of same disease group who didn't received GnRH-a^[84]. In important issue remains in fertility preservation where the ovary itself is the primary site of disease in ESFT and rarely ESFT can metastasize to the ovary^[85-87].

CONCLUSION

ESFTs are a rare aggressive tumor with high rate of

metastasis at presentation and high incidence of recurrence. The outcome of those with localized improved to 70% after multimodality approach mainly by better understanding of disease biology, risk adapted chemotherapeutic approach, timely incorporation of local therapy, and improvement in technology. But, the outcome of those with metastatic and recurrent disease is dismal and no significant advancement has been made in these patients to improve outcome in last four decades. The overall improvement in outcome of ESFT has been made through the tremendous efforts of researcher, clinicians all over the world, better liaison between all the stakeholders of treating team, and collaborative international research in a huge number of cases. The main challenge now remains in preventing recurrence, preventing drug resistance, reducing therapy related long-term toxicities and improving outcome in those with metastatic and relapsed/recurrent disease. No potential biomarker has been identified so far to predict therapeutic efficacy of chemotherapeutic agents and predicting recurrences. The future hope lies in finding useful biomarker, better understanding of disease biology and chemotherapy resistance of ESFT cells, proper designing and execution of targeted therapies currently going under clinical trials, better use of high throughput method to detect novel driver mutations/pathways and potential targets. Better selection of risk group and designing of trials combining chemotherapeutic agents with targeted therapies to bypass drug resistance along with judicious use of high dose chemotherapies, selection of more non-toxic agents with high efficacy and broad therapeutic windows will help to improve future outcomes in expense of decreased treatment related long-term toxicities and good quality of life in survivors.

REFERENCES

- 1 **Damron TA**, Ward WG, Stewart A. Osteosarcoma, chondrosarcoma, and Ewing's sarcoma: National Cancer Data Base Report. *Clin Orthop Relat Res* 2007; **459**: 40-47 [PMID: 17414166 DOI: 10.1097/BLO.0b013e318059b8e9]
- 2 **Biswas B**, Rastogi S, Khan SA, Shukla NK, Deo SV, Agarwala S, Sharma DN, Thulkar S, Vishnubhatla S, Pathania S, Bakhshi S. Hypoalbuminaemia is an independent predictor of poor outcome in metastatic Ewing's sarcoma family of tumours: a single institutional experience of 150 cases treated with uniform chemotherapy protocol. *Clin Oncol (R Coll Radiol)* 2014; **26**: 722-729 [PMID: 24919857 DOI: 10.1016/j.clon.2014.05.006]
- 3 **Cotterill SJ**, Ahrens S, Paulussen M, Jürgens HF, Voûte PA, Gardner H, Craft AW. Prognostic factors in Ewing's tumor of bone: analysis of 975 patients from the European Intergroup Cooperative Ewing's Sarcoma Study Group. *J Clin Oncol* 2000; **18**: 3108-3114 [PMID: 10963639]
- 4 **Delattre O**, Zucman J, Plougastel B, Desmaze C, Melot T, Peter M, Kovar H, Joubert I, de Jong P, Rouleau G. Gene fusion with an ETS DNA-binding domain caused by chromosome translocation in human tumours. *Nature* 1992; **359**: 162-165 [PMID: 1522903 DOI: 10.1038/359162a0]
- 5 **Gaspar N**, Di Giannatale A, Georger B, Redini F, Corradini N, Enz-Werle N, Tirode F, Marec-Berard P, Gentet JC, Laurence V, Piperno-Neumann S, Oberlin O, Brugieres L. Bone sarcomas: from biology to targeted therapies. *Sarcoma* 2012; **2012**: 301975 [PMID: 23226965 DOI: 10.1155/2012/301975]
- 6 **Grier HE**, Krailo MD, Tarbell NJ, Link MP, Fryer CJ, Pritchard

- DJ, Gebhardt MC, Dickman PS, Perlman EJ, Meyers PA, Donaldson SS, Moore S, Rausen AR, Vietti TJ, Miser JS. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. *N Engl J Med* 2003; **348**: 694-701 [PMID: 12594313 DOI: 10.1056/NEJMoa020890]
- 7 **Paulussen M**, Craft AW, Lewis I, Hackshaw A, Douglas C, Dunst J, Schuck A, Winkelmann W, Köhler G, Poremba C, Zoubek A, Ladenstein R, van den Berg H, Hunold A, Cassoni A, Spooner D, Grimer R, Whelan J, McTiernan A, Jürgens H. Results of the EICES-92 Study: two randomized trials of Ewing's sarcoma treatment--cyclophosphamide compared with ifosfamide in standard-risk patients and assessment of benefit of etoposide added to standard treatment in high-risk patients. *J Clin Oncol* 2008; **26**: 4385-4393 [PMID: 18802150 DOI: 10.1200/JCO.2008.16.5720]
 - 8 **Oberlin O**, Rey A, Desfachelles AS, Philip T, Plantaz D, Schmitt C, Plouvier E, Lejars O, Rubie H, Terrier P, Michon J. Impact of high-dose busulfan plus melphalan as consolidation in metastatic Ewing tumors: a study by the Société Française des Cancérs de l'Enfant. *J Clin Oncol* 2006; **24**: 3997-4002 [PMID: 16921053 DOI: 10.1200/JCO.2006.05.7059]
 - 9 **Luksch R**, Tienghi A, Hall KS, Fagioli F, Picci P, Barbieri E, Gandola L, Eriksson M, Ruggieri P, Daolio P, Lindholm P, Prete A, Bisogno G, Tamburini A, Grignani G, Abate ME, Podda M, Smeland S, Ferrari S. Primary metastatic Ewing's family tumors: results of the Italian Sarcoma Group and Scandinavian Sarcoma Group ISG/SSG IV Study including myeloablative chemotherapy and total-lung irradiation. *Ann Oncol* 2012; **23**: 2970-2976 [PMID: 22771824 DOI: 10.1093/annonc/nds117]
 - 10 **Ladenstein R**, Pötschger U, Le Deley MC, Whelan J, Paulussen M, Oberlin O, van den Berg H, Dirksen U, Hjorth L, Michon J, Lewis I, Craft A, Jürgens H. Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. *J Clin Oncol* 2010; **28**: 3284-3291 [PMID: 20547982 DOI: 10.1200/JCO.2009.22.9864]
 - 11 **Krasin MJ**, Rodriguez-Galindo C, Davidoff AM, Billups CA, Fuller CE, Neel MD, Kun LE, Merchant TE. Efficacy of combined surgery and irradiation for localized Ewing's sarcoma family of tumors. *Pediatr Blood Cancer* 2004; **43**: 229-236 [PMID: 15266406 DOI: 10.1002/pbc.20095]
 - 12 **Göbel V**, Jürgens H, Etspüler G, Kemperdick H, Jungblut RM, Stienen U, Göbel U. Prognostic significance of tumor volume in localized Ewing's sarcoma of bone in children and adolescents. *J Cancer Res Clin Oncol* 1987; **113**: 187-191 [PMID: 3558454 DOI: 10.1007/BF00391442]
 - 13 **Oberlin O**, Deley MC, Bui BN, Gentet JC, Philip T, Terrier P, Carrie C, Mechinaud F, Schmitt C, Babin-Boilletot A, Michon J. Prognostic factors in localized Ewing's tumours and peripheral neuroectodermal tumours: the third study of the French Society of Paediatric Oncology (EW88 study). *Br J Cancer* 2001; **85**: 1646-1654 [PMID: 11742482 DOI: 10.1054/bjoc.2001.2150]
 - 14 **Biswas B**, Rastogi S, Khan SA, Shukla NK, Deo SV, Agarwala S, Mohanti BK, Sharma MC, Vishnubhatla S, Bakhshi S. Developing a prognostic model for localized Ewing sarcoma family of tumors: A single institutional experience of 224 cases treated with uniform chemotherapy protocol. *J Surg Oncol* 2015; **111**: 683-689 [PMID: 25557999 DOI: 10.1002/jso.23861]
 - 15 **Le Deley MC**, Paulussen M, Lewis I, Brennan B, Ranft A, Whelan J, Le Teuff G, Michon J, Ladenstein R, Marec-Bérard P, van den Berg H, Hjorth L, Wheatley K, Judson I, Juergens H, Craft A, Oberlin O, Dirksen U. Cyclophosphamide compared with ifosfamide in consolidation treatment of standard-risk Ewing sarcoma: results of the randomized noninferiority Euro-EWING99-R1 trial. *J Clin Oncol* 2014; **32**: 2440-2448 [PMID: 24982464 DOI: 10.1200/JCO.2013.54.4833]
 - 16 **Biswas B**, Thakar A, Mohanti BK, Vishnubhatla S, Bakhshi S. Prognostic factors in head and neck Ewing sarcoma family of tumors. *Laryngoscope* 2015; **125**: E112-E117 [PMID: 25345585 DOI: 10.1002/lary.24985]
 - 17 **Biswas B**, Shukla NK, Deo SV, Agarwala S, Sharma DN, Vishnubhatla S, Bakhshi S. Evaluation of outcome and prognostic factors in extraosseous Ewing sarcoma. *Pediatr Blood Cancer* 2014; **61**: 1925-1931 [PMID: 25132242 DOI: 10.1002/pbc.25095]
 - 18 **Biswas B**, Rastogi S, Khan SA, Mohanti BK, Sharma DN, Sharma MC, Mridha AR, Bakhshi S. Outcomes and prognostic factors for Ewing-family tumors of the extremities. *J Bone Joint Surg Am* 2014; **96**: 841-849 [PMID: 24875025 DOI: 10.2106/JBJS.M.00411]
 - 19 **Zoubek A**, Dockhorn-Dworniczak B, Delattre O, Christiansen H, Niggli F, Gatterer-Menz I, Smith TL, Jürgens H, Gadner H, Kovar H. Does expression of different EWS chimeric transcripts define clinically distinct risk groups of Ewing tumor patients? *J Clin Oncol* 1996; **14**: 1245-1251 [PMID: 8648380]
 - 20 **de Alava E**, Lozano MD, Patiño A, Sierrasesúmaga L, Pardo-Mindán FJ. Ewing family tumors: potential prognostic value of reverse-transcriptase polymerase chain reaction detection of minimal residual disease in peripheral blood samples. *Diagn Mol Pathol* 1998; **7**: 152-157 [PMID: 9836070 DOI: 10.1097/00019606-199806000-00005]
 - 21 **van Doorninck JA**, Ji L, Schaub B, Shimada H, Wing MR, Krailo MD, Lessnick SL, Marina N, Triche TJ, Sposto R, Womer RB, Lawlor ER. Current treatment protocols have eliminated the prognostic advantage of type 1 fusions in Ewing sarcoma: a report from the Children's Oncology Group. *J Clin Oncol* 2010; **28**: 1989-1994 [PMID: 20308669 DOI: 10.1200/JCO.2009.24.5845]
 - 22 **Kovar H**, Alonso J, Aman P, Aryee DN, Ban J, Burchill SA, Burdach S, De Alava E, Delattre O, Dirksen U, Fourtouna A, Fulda S, Helman LJ, Herrero-Martin D, Hogendoorn PC, Kontny U, Lawlor ER, Lessnick SL, Llombart-Bosch A, Metzler M, Moriggl R, Niedan S, Potratz J, Redini F, Richter GH, Riedmann LT, Rossig C, Schäfer BW, Schwentner R, Scotlandi K, Sorensen PH, Staeger MS, Tirode F, Toretsky J, Ventura S, Eggert A, Ladenstein R. The first European interdisciplinary ewing sarcoma research summit. *Front Oncol* 2012; **2**: 54 [PMID: 22662320 DOI: 10.3389/fonc.2012.00054]
 - 23 **Tirode F**, Surdez D, Ma X, Parker M, Le Deley MC, Bahrami A, Zhang X, Lapouble E, Grossetête-Lalami S, Rusch M, Reynaud S, Rio-Frio T, Hedlund E, Wu G, Chen X, Pierron G, Oberlin O, Zaidi S, Lemmon G, Gupta P, Vadodaria B, Easton J, Gut M, Ding L, Mardis ER, Wilson RK, Shurtleff S, Laurence V, Michon J, Marec-Bérard P, Gut I, Downing J, Dyer M, Zhang J, Delattre O. Genomic landscape of Ewing sarcoma defines an aggressive subtype with co-association of STAG2 and TP53 mutations. *Cancer Discov* 2014; **4**: 1342-1353 [PMID: 25223734 DOI: 10.1158/2159-8290.CD-14-0622]
 - 24 **Schleiermacher G**, Delattre O. [Detection of micrometastases and circulating tumour cells using molecular biology techniques in solid tumours]. *Bull Cancer* 2001; **88**: 561-570 [PMID: 11459702]
 - 25 **Gupta K**, Pawaskar A, Basu S, Rajan MG, Asopa RV, Arora B, Nair N, Banavali S. Potential role of FDG PET imaging in predicting metastatic potential and assessment of therapeutic response to neoadjuvant chemotherapy in Ewing sarcoma family of tumors. *Clin Nucl Med* 2011; **36**: 973-977 [PMID: 21975382 DOI: 10.1097/RLU.0b013e31822f684b]
 - 26 **Hawkins DS**, Schuetze SM, Butrynski JE, Rajendran JG, Vernon CB, Conrad EU, Eary JF. [18F]Fluorodeoxyglucose positron emission tomography predicts outcome for Ewing sarcoma family of tumors. *J Clin Oncol* 2005; **23**: 8828-8834 [PMID: 16314643 DOI: 10.1200/JCO.2005.01.7079]
 - 27 **Gaston LL**, Di Bella C, Slavin J, Hicks RJ, Choong PF. 18F-FDG PET response to neoadjuvant chemotherapy for Ewing sarcoma and osteosarcoma are different. *Skeletal Radiol* 2011; **40**: 1007-1015 [PMID: 21298431 DOI: 10.1007/s00256-011-1096-4]
 - 28 **Nesbit ME**, Perez CA, Tefft M, Burgert EO, Vietti TJ, Kissane J, Pritchard DJ, Gehan EA. Multimodal therapy for the management of primary, nonmetastatic Ewing's sarcoma of bone: an Intergroup Study. *Natl Cancer Inst Monogr* 1981; **255**: 255-262 [PMID: 7029293]
 - 29 **Burgert EO**, Nesbit ME, Garnsey LA, Gehan EA, Herrmann J, Vietti TJ, Cangir A, Tefft M, Evans R, Thomas P. Multimodal therapy for the management of nonpelvic, localized Ewing's sarcoma of bone: intergroup study IEES-II. *J Clin Oncol* 1990; **8**: 1514-1524 [PMID: 2099751]

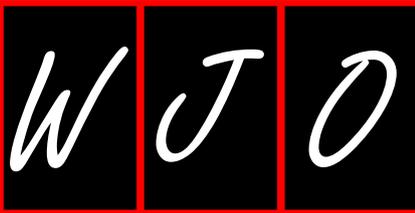
- 30 **Carli M**, Passone E, Perilongo G, Bisogno G. Ifosfamide in pediatric solid tumors. *Oncology* 2003; **65** Suppl 2: 99-104 [PMID: 14586158]
- 31 **Oberlin O**, Habrand JL, Zucker JM, Brunat-Mentigny M, Terrier-Lacombe MJ, Duboussset J, Gentet JC, Schmitt C, Ponvert D, Carrié C. No benefit of ifosfamide in Ewing's sarcoma: a nonrandomized study of the French Society of Pediatric Oncology. *J Clin Oncol* 1992; **10**: 1407-1412 [PMID: 1517783]
- 32 **Granowetter L**, Womer R, Devidas M, Krailo M, Wang C, Bernstein M, Marina N, Leavey P, Gebhardt M, Healey J, Shamberger RC, Goorin A, Miser J, Meyer J, Arndt CA, Sailer S, Marcus K, Perlman E, Dickman P, Grier HE. Dose-intensified compared with standard chemotherapy for nonmetastatic Ewing sarcoma family of tumors: a Children's Oncology Group Study. *J Clin Oncol* 2009; **27**: 2536-2541 [PMID: 19349548 DOI: 10.1200/JCO.2008.19.1478]
- 33 **Womer RB**, West DC, Krailo MD, Dickman PS, Pawel BR, Grier HE, Marcus K, Sailer S, Healey JH, Dormans JP, Weiss AR. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: a report from the Children's Oncology Group. *J Clin Oncol* 2012; **30**: 4148-4154 [PMID: 23091096 DOI: 10.1200/JCO.2011.41.5703]
- 34 **Ferrari S**, Sundby Hall K, Luksch R, Tienghi A, Wiebe T, Fagioli F, Alvegard TA, Brach Del Prever A, Tamburini A, Alberghini M, Gandola L, Mercuri M, Capanna R, Mapelli S, Prete A, Carli M, Picci P, Barbieri E, Bacci G, Smeland S. Nonmetastatic Ewing family tumors: high-dose chemotherapy with stem cell rescue in poor responder patients. Results of the Italian Sarcoma Group/Scandinavian Sarcoma Group III protocol. *Ann Oncol* 2011; **22**: 1221-1227 [PMID: 21059639 DOI: 10.1093/annonc/mdq573]
- 35 **Gaspar N**, Rey A, Bérard PM, Michon J, Gentet JC, Tabone MD, Roché H, Defachelles AS, Lejars O, Plouvier E, Schmitt C, Bui B, Boutard P, Taque S, Munzer M, Vannier JP, Plantaz D, Entz-Werle N, Oberlin O. Risk adapted chemotherapy for localised Ewing's sarcoma of bone: the French EW93 study. *Eur J Cancer* 2012; **48**: 1376-1385 [PMID: 22516209 DOI: 10.1016/j.ejca.2012.03.017]
- 36 **DuBois SG**, Krailo MD, Gebhardt MC, Donaldson SS, Marcus KJ, Dormans J, Shamberger RC, Sailer S, Nicholas RW, Healey JH, Tarbell NJ, Randall RL, Devidas M, Meyer JS, Granowetter L, Womer RB, Bernstein M, Marina N, Grier HE. Comparative evaluation of local control strategies in localized Ewing sarcoma of bone: a report from the Children's Oncology Group. *Cancer* 2015; **121**: 467-475 [PMID: 25251206 DOI: 10.1002/cncr.29065]
- 37 **Hardes J**, von Eiff C, Streitbuenger A, Balke M, Budny T, Henrichs MP, Hauschild G, Ahrens H. Reduction of periprosthetic infection with silver-coated megaprotheses in patients with bone sarcoma. *J Surg Oncol* 2010; **101**: 389-395 [PMID: 20119985 DOI: 10.1002/jso.21498]
- 38 **Craft AW**, Cotterill SJ, Bullimore JA, Pearson D. Long-term results from the first UKCCSG Ewing's Tumour Study (ET-1). United Kingdom Children's Cancer Study Group (UKCCSG) and the Medical Research Council Bone Sarcoma Working Party. *Eur J Cancer* 1997; **33**: 1061-1069 [PMID: 9376188]
- 39 **Donaldson SS**, Torrey M, Link MP, Glicksman A, Gilula L, Laurie F, Manning J, Neff J, Reinius W, Thompson E, Shuster JJ. A multidisciplinary study investigating radiotherapy in Ewing's sarcoma: end results of POG #8346. Pediatric Oncology Group. *Int J Radiat Oncol Biol Phys* 1998; **42**: 125-135 [PMID: 9747829 DOI: 10.1016/S0360-3016(98)00191-6]
- 40 **Schuck A**, Rube C, Koenemann S, Rube CE, Ahrens S, Paulussen M, Dunst J, Jürgens H, Willich N. Postoperative radiotherapy in the treatment of Ewing tumors: influence of the interval between surgery and radiotherapy. *Strahlenther Onkol* 2002; **178**: 25-31 [PMID: 11977388 DOI: 10.1007/s00066-002-0883-1]
- 41 **Schuck A**, Ahrens S, Paulussen M, Kuhlen M, Koenemann S, Rube C, Winkelmann W, Kotz R, Dunst J, Willich N, Jürgens H. Local therapy in localized Ewing tumors: results of 1058 patients treated in the CESS 81, CESS 86, and ECESS 92 trials. *Int J Radiat Oncol Biol Phys* 2003; **55**: 168-177 [PMID: 12504050 DOI: 10.1016/S0360-3016(02)03797-5]
- 42 **Bacci G**, Forni C, Longhi A, Ferrari S, Donati D, De Paolis M, Barbieri E, Pignotti E, Rosito P, Versari M. Long-term outcome for patients with non-metastatic Ewing's sarcoma treated with adjuvant and neoadjuvant chemotherapies. 402 patients treated at Rizzoli between 1972 and 1992. *Eur J Cancer* 2004; **40**: 73-83 [PMID: 14687792]
- 43 **Shankar AG**, Pinkerton CR, Atra A, Ashley S, Lewis I, Spooner D, Cannon S, Grimer R, Cotterill SJ, Craft AW. Local therapy and other factors influencing site of relapse in patients with localised Ewing's sarcoma. United Kingdom Children's Cancer Study Group (UKCCSG). *Eur J Cancer* 1999; **35**: 1698-1704 [PMID: 10674016]
- 44 **Obata H**, Ueda T, Kawai A, Ishii T, Ozaki T, Abe S, Tanaka K, Tsuchiya H, Matsumine A, Yabe H. Clinical outcome of patients with Ewing sarcoma family of tumors of bone in Japan: the Japanese Musculoskeletal Oncology Group cooperative study. *Cancer* 2007; **109**: 767-775 [PMID: 17238190 DOI: 10.1002/cncr.22481]
- 45 **Rodriguez-Galindo C**, Navid F, Liu T, Billups CA, Rao BN, Krasin MJ. Prognostic factors for local and distant control in Ewing sarcoma family of tumors. *Ann Oncol* 2008; **19**: 814-820 [PMID: 17998282 DOI: 10.1093/annonc/mdm521]
- 46 **Lee J**, Hoang BH, Ziogas A, Zell JA. Analysis of prognostic factors in Ewing sarcoma using a population-based cancer registry. *Cancer* 2010; **116**: 1964-1973 [PMID: 20151425 DOI: 10.1002/cncr.24937]
- 47 **Biswas B**, Agarwala S, Rastogi S, Khan SA, Mohanti BK, Sharma DN, Pathy S, Bakhshi S. High burden of metastases and poor outcome in pelvic PNET. *Pediatr Blood Cancer* 2013; **60**: E97-E99 [PMID: 23625700 DOI: 10.1002/pbc.24552]
- 48 **Paulussen M**, Ahrens S, Craft AW, Dunst J, Fröhlich B, Jabar S, Rube C, Winkelmann W, Wissing S, Zoubek A, Jürgens H. Ewing's tumors with primary lung metastases: survival analysis of 114 (European Intergroup) Cooperative Ewing's Sarcoma Studies patients. *J Clin Oncol* 1998; **16**: 3044-3052 [PMID: 9738574]
- 49 **Juergens C**, Weston C, Lewis I, Whelan J, Paulussen M, Oberlin O, Michon J, Zoubek A, Juergens H, Craft A. Safety assessment of intensive induction with vincristine, ifosfamide, doxorubicin, and etoposide (VIDE) in the treatment of Ewing tumors in the EURO-E. W.I.N.G. 99 clinical trial. *Pediatr Blood Cancer* 2006; **47**: 22-29 [PMID: 16572419 DOI: 10.1002/pbc.20820]
- 50 **Casey DL**, Wexler LH, Meyers PA, Magnost H, Chou AJ, Wolden SL. Radiation for bone metastases in Ewing sarcoma and rhabdomyosarcoma. *Pediatr Blood Cancer* 2015; **62**: 445-449 [PMID: 25346208 DOI: 10.1002/pbc.25294]
- 51 **Heij HA**, Vos A, de Kraker J, Voûte PA. Prognostic factors in surgery for pulmonary metastases in children. *Surgery* 1994; **115**: 687-693 [PMID: 8197559]
- 52 **Bacci G**, Briccoli A, Picci P, Ferrari S. Metachronous pulmonary metastases resection in patients with Ewing's sarcoma initially treated with adjuvant or neoadjuvant chemotherapy. *Eur J Cancer* 1995; **31A**: 999-1001 [PMID: 7646936]
- 53 **Ladenstein R**, Hartmann O, Pinkerton CR. The role of megatherapy with autologous bone marrow rescue in solid tumours of childhood. *Ann Oncol* 1993; **4** Suppl 1: 45-58 [PMID: 8338795 DOI: 10.1093/annonc/4.suppl_1.S45]
- 54 **Meyers PA**, Krailo MD, Ladanyi M, Chan KW, Sailer SL, Dickman PS, Baker DL, Davis JH, Gerbing RB, Grovas A, Herzog CE, Lindsley KL, Liu-Mares W, Nachman JB, Sieger L, Wadman J, Gorlick RG. High-dose melphalan, etoposide, total-body irradiation, and autologous stem-cell reconstitution as consolidation therapy for high-risk Ewing's sarcoma does not improve prognosis. *J Clin Oncol* 2001; **19**: 2812-2820 [PMID: 11387352]
- 55 **Yock TI**, Krailo M, Fryer CJ, Donaldson SS, Miser JS, Chen Z, Bernstein M, Laurie F, Gebhardt MC, Grier HE, Tarbell NJ. Local control in pelvic Ewing sarcoma: analysis from INT-0091--a report from the Children's Oncology Group. *J Clin Oncol* 2006; **24**: 3838-3843 [PMID: 16921035 DOI: 10.1200/JCO.2006.05.9188]
- 56 **Rodriguez-Galindo C**, Billups CA, Kun LE, Rao BN, Pratt CB, Merchant TE, Santana VM, Pappo AS. Survival after recurrence of Ewing tumors: the St Jude Children's Research Hospital experience,

- 1979-1999. *Cancer* 2002; **94**: 561-569 [PMID: 11900241 DOI: 10.1002/cncr.10192]
- 57 **Hunold A**, Weddeling N, Paulussen M, Ranft A, Liebscher C, Jürgens H. Topotecan and cyclophosphamide in patients with refractory or relapsed Ewing tumors. *Pediatr Blood Cancer* 2006; **47**: 795-800 [PMID: 16411206 DOI: 10.1002/pbc.20719]
- 58 **Van Winkle P**, Angiolillo A, Krailo M, Cheung YK, Anderson B, Davenport V, Reaman G, Cairo MS. Ifosfamide, carboplatin, and etoposide (ICE) reinduction chemotherapy in a large cohort of children and adolescents with recurrent/refractory sarcoma: the Children's Cancer Group (CCG) experience. *Pediatr Blood Cancer* 2005; **44**: 338-347 [PMID: 15503297 DOI: 10.1002/pbc.20227]
- 59 **Wagner LM**, Crews KR, Iacono LC, Houghton PJ, Fuller CE, McCarville MB, Goldsby RE, Albritton K, Stewart CF, Santana VM. Phase I trial of temozolomide and protracted irinotecan in pediatric patients with refractory solid tumors. *Clin Cancer Res* 2004; **10**: 840-848 [PMID: 14871959 DOI: 10.1158/1078-0432.CCR-03-0175]
- 60 **Fox E**, Patel S, Wathen JK, Schuetze S, Chawla S, Harmon D, Reinke D, Chugh R, Benjamin RS, Helman LJ. Phase II study of sequential gemcitabine followed by docetaxel for recurrent Ewing sarcoma, osteosarcoma, or unresectable or locally recurrent chondrosarcoma: results of Sarcoma Alliance for Research Through Collaboration Study 003. *Oncologist* 2012; **17**: 321 [PMID: 22363068 DOI: 10.1634/theoncologist.2010-0265]
- 61 **Casey DA**, Wexler LH, Merchant MS, Chou AJ, Merola PR, Price AP, Meyers PA. Irinotecan and temozolomide for Ewing sarcoma: the Memorial Sloan-Kettering experience. *Pediatr Blood Cancer* 2009; **53**: 1029-1034 [PMID: 19637327 DOI: 10.1002/pbc.22206]
- 62 **Wagner LM**, McAllister N, Goldsby RE, Rausen AR, McNall-Knapp RY, McCarville MB, Albritton K. Temozolomide and intravenous irinotecan for treatment of advanced Ewing sarcoma. *Pediatr Blood Cancer* 2007; **48**: 132-139 [PMID: 16317751 DOI: 10.1002/pbc.20697]
- 63 **Raciborska A**, Biliska K, Drabko K, Chaber R, Pogorzala M, Wyrobek E, Polczyńska K, Rogowska E, Rodriguez-Galindo C, Wozniak W. Vincristine, irinotecan, and temozolomide in patients with relapsed and refractory Ewing sarcoma. *Pediatr Blood Cancer* 2013; **60**: 1621-1625 [PMID: 23776128 DOI: 10.1002/pbc.24621]
- 64 **McNall-Knapp RY**, Williams CN, Reeves EN, Heideman RL, Meyer WH. Extended phase I evaluation of vincristine, irinotecan, temozolomide, and antibiotic in children with refractory solid tumors. *Pediatr Blood Cancer* 2010; **54**: 909-915 [PMID: 20405511 DOI: 10.1002/pbc.22460]
- 65 **Kurucu N**, Sari N, Ilhan IE. Irinotecan and temozolamide treatment for relapsed Ewing sarcoma: a single-center experience and review of the literature. *Pediatr Hematol Oncol* 2015; **32**: 50-59 [PMID: 25252096 DOI: 10.3109/08880018.2014.954070]
- 66 **Gardner SL**, Carreras J, Boudreau C, Camitta BM, Adams RH, Chen AR, Davies SM, Edwards JR, Grovas AC, Hale GA, Lazarus HM, Arora M, Stiff PJ, Eapen M. Myeloablative therapy with autologous stem cell rescue for patients with Ewing sarcoma. *Bone Marrow Transplant* 2008; **41**: 867-872 [PMID: 18246113 DOI: 10.1038/bmt.2008.2]
- 67 **McTiernan A**, Driver D, Michelagnoli MP, Kilby AM, Whelan JS. High dose chemotherapy with bone marrow or peripheral stem cell rescue is an effective treatment option for patients with relapsed or progressive Ewing's sarcoma family of tumours. *Ann Oncol* 2006; **17**: 1301-1305 [PMID: 16782749 DOI: 10.1093/annonc/mdl108]
- 68 **Erkizan HV**, Scher LJ, Gamble SE, Barber-Rotenberg JS, Sajwan KP, Üren A, Toretzky JA. Novel peptide binds EWS-FLI1 and reduces the oncogenic potential in Ewing tumors. *Cell Cycle* 2011; **10**: 3397-3408 [PMID: 21926473 DOI: 10.4161/cc.10.19.17734]
- 69 **Boro A**, Prêtre K, Rechfeld F, Thalhammer V, Oesch S, Wachtel M, Schäfer BW, Niggli FK. Small-molecule screen identifies modulators of EWS/FLI1 target gene expression and cell survival in Ewing's sarcoma. *Int J Cancer* 2012; **131**: 2153-2164 [PMID: 22323082 DOI: 10.1002/ijc.27472]
- 70 **Grohar PJ**, Griffin LB, Yeung C, Chen QR, Pommier Y, Khanna C, Khan J, Helman LJ. Ecteinascidin 743 interferes with the activity of EWS-FLI1 in Ewing sarcoma cells. *Neoplasia* 2011; **13**: 145-153 [PMID: 21403840 DOI: 10.1593/neo.101202]
- 71 **Glade Bender JL**, Lee A, Reid JM, Baruchel S, Roberts T, Voss SD, Wu B, Ahern CH, Ingle AM, Harris P, Weigel BJ, Blaney SM. Phase I pharmacokinetic and pharmacodynamic study of pazopanib in children with soft tissue sarcoma and other refractory solid tumors: a children's oncology group phase I consortium report. *J Clin Oncol* 2013; **31**: 3034-3043 [PMID: 23857966 DOI: 10.1200/JCO.2012.47.0914]
- 72 **Wittrant Y**, Théoleyre S, Chipoy C, Padrines M, Blanchard F, Heymann D, Rédini F. RANKL/RANK/OPG: new therapeutic targets in bone tumours and associated osteolysis. *Biochim Biophys Acta* 2004; **1704**: 49-57 [PMID: 15363860 DOI: 10.1016/j.bbcan.2004.05.002]
- 73 **Odri GA**, Dumoucel S, Picarda G, Battaglia S, Lamoureux F, Corradini N, Rousseau J, Tirode F, Laud K, Delattre O, Gouin F, Heymann D, Redini F. Zoledronic acid as a new adjuvant therapeutic strategy for Ewing's sarcoma patients. *Cancer Res* 2010; **70**: 7610-7619 [PMID: 20841471 DOI: 10.1158/0008-5472.CAN-09-4272]
- 74 **Garofalo C**, Mancarella C, Grilli A, Manara MC, Astolfi A, Marino MT, Conte A, Sigismund S, Carè A, Belfiore A, Picci P, Scotlandi K. Identification of common and distinctive mechanisms of resistance to different anti-IGF-IR agents in Ewing's sarcoma. *Mol Endocrinol* 2012; **26**: 1603-1616 [PMID: 22798295 DOI: 10.1210/me.2012-1142]
- 75 **Brenner JC**, Feng FY, Han S, Patel S, Goyal SV, Bou-Maroun LM, Liu M, Lonigro R, Prensner JR, Tomlins SA, Chinnaiyan AM. PARP-1 inhibition as a targeted strategy to treat Ewing's sarcoma. *Cancer Res* 2012; **72**: 1608-1613 [PMID: 22287547 DOI: 10.1158/0008-5472.CAN-11-3648]
- 76 **Kailayangiri S**, Altvater B, Meltzer J, Pscherer S, Luecke A, Dierkes C, Titze U, Leuchte K, Landmeier S, Hotfilder M, Dirksen U, Harges J, Gosheger G, Juergens H, Rossig C. The ganglioside antigen G(D2) is surface-expressed in Ewing sarcoma and allows for MHC-independent immune targeting. *Br J Cancer* 2012; **106**: 1123-1133 [PMID: 22374462 DOI: 10.1038/bjc.2012.57]
- 77 **Scotlandi K**, Perdichizzi S, Bernard G, Nicoletti G, Nanni P, Lollini PL, Curti A, Manara MC, Benini S, Bernard A, Picci P. Targeting CD99 in association with doxorubicin: an effective combined treatment for Ewing's sarcoma. *Eur J Cancer* 2006; **42**: 91-96 [PMID: 16326096 DOI: 10.1016/j.ejca.2005.09.015]
- 78 **Chemaitilly W**, Mertens AC, Mitby P, Whitton J, Stovall M, Yasui Y, Robison LL, Sklar CA. Acute ovarian failure in the childhood cancer survivor study. *J Clin Endocrinol Metab* 2006; **91**: 1723-1728 [PMID: 16492690 DOI: 10.1210/jc.2006-0020]
- 79 **Frederick JL**, Ord T, Kettel LM, Stone SC, Balmaceda JP, Asch RH. Successful pregnancy outcome after cryopreservation of all fresh embryos with subsequent transfer into an unstimulated cycle. *Fertil Steril* 1995; **64**: 987-990 [PMID: 7589647 DOI: 10.1016/S0015-0282(16)57915-1]
- 80 **Sonmezer M**, Oktay K. Fertility preservation in female patients. *Hum Reprod Update* 2004; **10**: 251-266 [PMID: 15140872 DOI: 10.1093/humupd/dmh021]
- 81 **Meirow D**, Levron J, Eldar-Geva T, Hardan I, Fridman E, Zalel Y, Schiff E, Dor J. Pregnancy after transplantation of cryopreserved ovarian tissue in a patient with ovarian failure after chemotherapy. *N Engl J Med* 2005; **353**: 318-321 [PMID: 15983020 DOI: 10.1056/NEJMc055237]
- 82 **Silber SJ**, Lenahan KM, Levine DJ, Pineda JA, Gorman KS, Friez MJ, Crawford EC, Gosden RG. Ovarian transplantation between monozygotic twins discordant for premature ovarian failure. *N Engl J Med* 2005; **353**: 58-63 [PMID: 15941849 DOI: 10.1056/NEJMoa043157]
- 83 **Husseinzadeh N**, Nahhas WA, Velkley DE, Whitney CW, Mortel R. The preservation of ovarian function in young women undergoing pelvic radiation therapy. *Gynecol Oncol* 1984; **18**: 373-379 [PMID: 6430756 DOI: 10.1016/0090-8258(84)90049-0]
- 84 **Blumenfeld Z**, Avivi I, Linn S, Epelbaum R, Ben-Shahar M, Haim N. Prevention of irreversible chemotherapy-induced ovarian damage

- in young women with lymphoma by a gonadotrophin-releasing hormone agonist in parallel to chemotherapy. *Hum Reprod* 1996; **11**: 1620-1626 [PMID: 8921104 DOI: 10.1093/oxfordjournals.humrep.a019457]
- 85 **Abir R**, Feinmesser M, Yaniv I, Fisch B, Cohen IJ, Ben-Haroush A, Meirow D, Felz C, Avigad S. Occasional involvement of the ovary in Ewing sarcoma. *Hum Reprod* 2010; **25**: 1708-1712 [PMID: 20472912 DOI: 10.1093/humrep/deq121]
- 86 **Sullivan HC**, Shulman SC, Olson T, Ricketts R, Oskouei S, Shehata BM. Unusual presentation of metastatic Ewing sarcoma to the ovary in a 13 year-old: a case report and review. *Fetal Pediatr Pathol* 2012; **31**: 159-163 [PMID: 22413993 DOI: 10.3109/15513815.2012.659379]
- 87 **Young RH**, Scully RE. Sarcomas metastatic to the ovary: a report of 21 cases. *Int J Gynecol Pathol* 1990; **9**: 231-252 [PMID: 2373588 DOI: 10.1097/00004347-199007000-00004]

P- Reviewer: Blumenfeld Z, Mocellin S, Romani A, Shimoyama S
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D





Casting: Pearls and pitfalls learned while caring for children's fractures

Shawn Nguyen, Mitchell McDowell, John Schlechter

Shawn Nguyen, John Schlechter, Department of Orthopaedic Surgery, Riverside University Health Sciences, Moreno Valley, CA 92555, United States

Mitchell McDowell, Department of Orthopaedic Surgery, Kaiser Permanente - Moreno Valley, Moreno Valley, CA 92555, United States

Author contributions: Nguyen S wrote the manuscript; McDowell M and Schlechter J reviewed and edited the manuscript.

Conflict-of-interest statement: Authors declare no conflict of interests for this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Shawn Nguyen, DO, Department of Orthopaedic Surgery, Riverside University Health Sciences, 26520 Cactus Ave., Moreno Valley, CA 92555, United States. shawnvnguyen@gmail.com
Telephone: +1-714-3572668
Fax: +1-951-4864106

Received: April 28, 2016

Peer-review started: April 29, 2016

First decision: June 17, 2016

Revised: July 1, 2016

Accepted: July 20, 2016

Article in press: July 22, 2016

Published online: September 18, 2016

is to provide pearls and pitfalls that our institution has learned from previous literature. When applying the cast, we recommend using cotton padding for the liner and fiberglass or plaster depending on how much swelling is expected. A well-molded cast must be applied in order to prevent further fracture displacement. Cast valving is a valuable technique that allows a decrease in pressure which prevents discomfort and complications like compartment syndrome. Preventing thermal injuries, skin complications, and a wet cast are other important considerations when caring for casts. Appropriate use of a cast saw, avoiding pressure spots, and properly covering the cast are ways to respectively prevent those complications. Lastly, patient education remains one of the most valuable tools in ensuring proper cast maintenance.

Key words: Cast care; Fracture cast; Pediatric casting; Pediatric fractures; Casting; Cast complications

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Casting is a routine procedure used for fracture care in the adult and pediatric population. The pediatric population present a unique set of attributes that often making casting difficult. In this article we will review different pearls and pitfalls seen while treating fractures in children which includes cast application, maintenance, and removal.

Nguyen S, McDowell M, Schlechter J. Casting: Pearls and pitfalls learned while caring for children's fractures. *World J Orthop* 2016; 7(9): 539-545 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/539.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.539>

Abstract

Casting is a routine procedure used for fracture care in the pediatric population. The purpose of this review

INTRODUCTION

Casting is a routine procedure used for fracture care in the pediatric population. Casting may be performed to

immobilize non-displaced fractures, maintain reduction of displaced fractures and protect operatively treated fractures. As commonly as casting is performed, the art of this technique appears to be less emphasized in many orthopaedic training programs, especially with the advancement in methods of surgical fixation of children's fractures. However, their use remains as a mainstay in orthopedics. Orthopaedic providers with a wide range of training background (*i.e.*, physician assistants, nurse practitioners, cast technicians) often are the primary applicators of a cast. Despite casting being performed by a wide range of providers, it should not be viewed as a procedure without risks.

Numerous studies, historical and recent, have looked at common complications of casting^[1-11]. Many of these have focused on hip spica casts and forearm fractures treated with short or long arm casts^[12-16]. These complications can range from skin excoriations to compartment syndrome.

Complications and improper application of casts have contributed a burden of non-emergent patients seen in emergency departments^[17]. Sawyer *et al.*^[17] investigated patients that are seen in emergency departments for problems relative to their cast and found that approximately 29% of the visits were because of a wet cast; 10%, were secondary to a damaged cast; 23%, a tight cast; 13%, a loose cast; and 10%, new or different pain. When casting has been applied correctly, it has the potential to save a significant amount of money when compared to surgical alternatives^[17]. According to Newton and Mubarak, the total charges for a hip spica were \$494 while the surgical alternative was approximately \$21000^[18].

The purpose of this article is to review the current literature pertinent to casting and share our own pearls and pitfalls that we have learned while caring for children's fractures with a cast. We also aim to provide various recommendations to safely and effectively place, maintain, and remove casts.

CAST MATERIAL

One of the primary decisions the provider has to make when applying a cast is what material to use. The two types that are traditionally used are plaster and fiberglass. Each of which have benefits and drawbacks that must be considered when choosing one over the other.

Plaster-impregnated cloth's major advantage includes its ability to mold more easily than its counterpart. This allows the provider to apply a custom mold to a reduced fracture and maintain reduction during the healing process. The drawbacks of plaster is it has a poor resistance to water and low strength-to-weight ratio which make it noticeably heavier than fiberglass^[19].

When treating fractures in children primarily with a cast, fiberglass is usually our preferred choice. Since the child on average will wear the cast for 4-6 wk, the lighter and less bulky fit often makes it more comfortable for

the child.

CAST APPLICATION

Cast application entails many elements which include the type and amount of material used, type of soft roll, presence or absence of stockinet and the method of rolling the cast as well as the final cast shape and position. The importance of a well-molded cast cannot be over emphasized^[12,20]. One of the main tenets of the cast application is to apply a mold based on the fracture pattern to, when applicable, maintain reduction and/or prevent displacement from occurring or at least worsening (Figure 1).

Excessive focused pressure over a small surface area of the cast can lead to decreased areas of perfusion and cause pressure sores. The practitioner should be constantly aware of their hand position in addition to the assistants' so they do not stay in one location for too long. Avoiding wrinkles and uneven ridges throughout the cast are details that will cause even pressure distribution throughout the extremity.

When treating distal radial and ulna fractures calculating the cast index on post application radiographs has been demonstrated to predict fracture displacement after cast application^[14,20-22] (Figure 2). The measure is performed at the level of the fracture. The goal is to create a ratio of sagittal width to coronal width to be equal or less than 0.8. If the ratio is equal or less than 0.8 the fracture has approximately 5% of displacement as opposed to 26% chance for an index greater than 0.8. Another radiographic measurement that can be used when treating fractures of the distal radius and ulna is an angle measured by the index finger or second-metacarpal and distal radius^[23]. To oppose the pull of the brachioradialis, which is often a deforming force in distal one-third radial fractures, molding a cast in ulnar deviation is recommended. If molded with ulnar deviation (second metacarpal-radius angle > 0 degrees), the outcome was considered to be ideal in 86.7% of cases compared to only 74.4% when it was < 0 degrees^[23].

Applying the index layer of fiberglass is crucial to ensuring a proper fit to the child's extremity. It is also important when needing a mold. If the index layer is applied too loosely, the cast will slide on the extremity when applying the mold and ultimately cause displacement of where the mold was originally intended for (Figure 3). However, if the index layer is applied too tightly, the obvious concern is soft tissue and vascular compromise. Our recommendation is that the material, whether plaster or fiberglass, be "un-rolled" onto the extremity to be casted and not pulled onto or wrapped in a fashion that can be constricting.

CAST VALVING AND PADDING

Cast valving and spreading is a technique that is employed in an attempt to alleviate pressure within a cast^[9,10,19,24]. A cast valve is performed using a cast



Figure 1 Well-molded cast. A: Pre-reduction X-rays of pediatric forearm demonstrating a completely displaced distal both bone forearm fracture. Immediate post-reduction X-rays; B: Immediate post-reduction X-rays demonstrating adequate reduction with a flexion mold to prevent fracture from dorsal displacement; C: Three-months follow-up X-rays demonstrating completely healed fracture with near-anatomic alignment.



Figure 2 Cast index. A: Initial X-rays of a pediatric forearm fracture with angulation; B: Immediate post-reduction X-rays demonstrating an appropriate cast application based on the cast index (< 0.8). Cast index = Sagittal width/coronal width = 41.4 mm/54.4 mm = 0.76.

saw to create a longitudinal linear cut parallel to the long axis of the limb. The cut is either left open with or without a space holder and may be secured by tape. This technique is commonly used after an acute injury, closed reduction, or immediately after surgical fixation all scenarios where the treated limb is at risk for further swelling.

Roberts *et al*^[6] performed a biomechanical study that evaluated the amount of pressure reduction after valving a cast in relation to different casting material. They compared effects of cotton, synthetic, and waterproof padding in addition to the effects of overwrapping a valved cast with an elastic bandage. They concluded that valving a cast with cotton padding beneath resulted in the greatest amount pressure reduction when compared to synthetic and waterproof padding and concluded that cotton padding demonstrated the greatest change in pressure within a long-arm cast after undergoing a bivalve. They stated that synthetic and waterproof cast padding should not be used in the setting of an acute fracture to accommodate swelling. Our custom and practice has been to use cotton padding in all instances because of its ease of use, ability to mold and trim in addition to better pressure reduction after valving as shown by Roberts *et al*^[6].

In warm climates especially during warmer months waterproof material is also an acceptable option especially when caring for sub-acute or non-displaced fractures. Robert *et al*^[25] designed a study that compared casts lined with cotton vs water-proof liners and their effectiveness on maintaining pediatric distal forearm fractures. The results showed that there was no significant difference in amount of displacement and angulation at final follow-up between the two groups and that waterproof liners were equally as effective in maintaining reduction.

When considering univalving vs bivalving, this decision is based on how much swelling the practitioner expects from the injury. Most low-to-medium energy trauma can be treated with a univalve, however children that have undergone a high-energy mechanism trauma, bivalving should be strongly considered in cases where casting is preferred over splinting. Zaino *et al*^[24] performed a study comparing the most effective method in decreasing method in reducing cast pressure in fiberglass casts. Their study concluded that the triple cut method which included bivalving, spreading, and cutting the cotton padding was the most effective in reducing clinically relevant skin pressure^[24].

Another useful tool that can be used when valving a



Figure 3 Loose cast. Pediatric cast that was applied too loosely. The physician's hand (right) was able to pull the cast off the child easily.

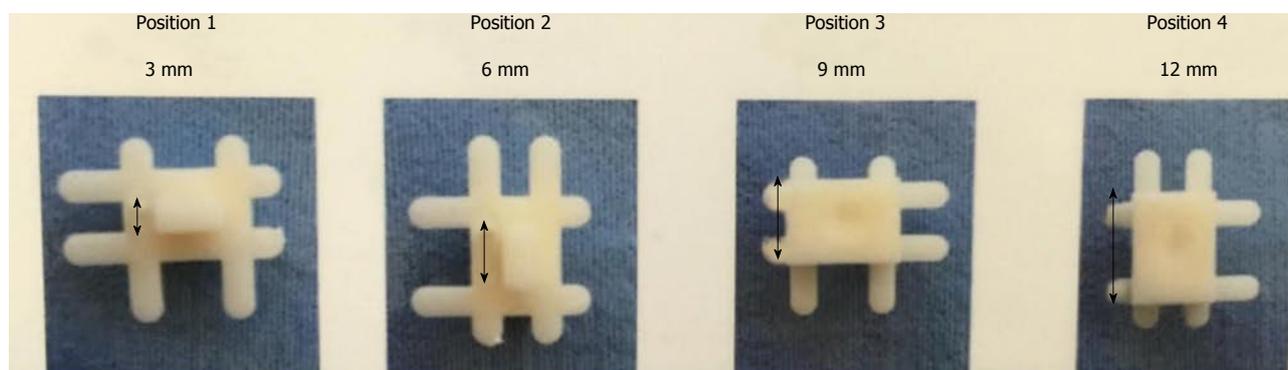


Figure 4 Cast spacers. Cast spacers with four different size settings (3, 6, 9 and 12 mm).

cast are commercially available cast spacers (Figure 4). These cast spacers are inserted in the valved area and are taped circumferentially around the cast. The purpose of the spacer is to maintain a constant spread in the cast material and diminish underlying pressure. The commercially available spacer we typically use has four different inserts that differ in size (3, 6, 9 or 12 mm) in which the provider can adjust the size of the space. Kleis *et al*^[26] recently presented their experimental findings after investigating the utility of spacer placement after cast valving. In their study model they reported reduction or pressure by 34% to 95% depending on the setting of the spacer. They recommended using Position #2 for most scenarios as it reduces pressure by an average of 78% but does not weaken the cast. For high energy traumas, Position #3 would be a safer option to prevent excessive compartment pressures.

It is customary for us to use cast spacers in every valved cast most often in the 6 mm position.

THERMAL INJURY

Burns caused after cast application have been studied in recent reports^[27,28]. The curing of the cast material itself is exothermic and heat producing. Although the occurrence is not a commonly encountered complication, an unnecessary heat exposure to the child can be uncomfortable and stressful. The risk of thermal injuries may be increased when the temperature of the dip water

for the cast material exceeds $> 50^{\circ}\text{C}$ or when the cast is too thick $> 24\text{-ply}$ ^[27,28].

Accurately measuring the dip water immediately prior to each cast application is possible but not highly feasible in most clinical scenarios. Dip water temperature should be warm to the touch similar to the temperature customary when bathing an infant. Although using warmer temperatures will allow the cast to harden at a faster rate, practitioners need to be aware that higher water temperature will increase the risk of thermal injury.

Cast thickness greater than 24-ply is difficult to achieve on most standard casts however the areas that are of concern are located on the concavities and flexion creases of the extremity. A natural surface area discrepancy is present when a cast is placed across a joint that is not in pure extension. These locations include the dorsal aspect of the ankle joint, posterior knee joint, and antecubital fossa of the elbow joint. In these locations a 1:2, concave: Convex ratio is recommended when applying material in these areas. This will prevent excess layers in the areas that are prone to thermal injury.

Another important aspect of preventing thermal injury during casting is to ensure the cast is completely hardened before supporting the extremity on a pillow or soft blanket^[27]. If the un-hardened cast is placed on a pillow, the heat generated from the exothermic reaction in the material will be smothered, heat escape limited and the potential for thermal injury is increased.

PREVENTING A WET CAST

When a cast becomes wet, numerous complications can occur, which include skin maceration, infection, and disruption of the structural integrity of the cast^[29]. Although educating the patient and family regarding the importance of protecting their cast and keeping it dry is paramount the incidence of a wet cast still continues to be problematic^[17]. Currently, there are various methods and products whose purpose is to help prevent casts from becoming wet. These methods include commercially available cast protectors, waterproof liners, and a combination of household products.

McDowell *et al.*^[30] compared these various methods on their effectiveness in preventing water absorption when applied to a cast. In addition, they also evaluated the most cost effective method. They found that all of the methods provided some level of protection when the cast in their experimental model was exposed to water. They concluded that although abstaining from contact with water is the most prudent approach, if a cast cover is to be used, double plastic bags with duct tape (100% prevention, \$10) and the store bought cast protector (100% prevention, \$13) were their preferred contemporary methods to prevent a wet cast.

Waterproof padding or cast liners are another option for children to allow bathing or water based activities while in a cast. We have often found that the adding cost of these materials are not covered by most commercial insurers in the United State and often the cost of these materials are transferred to the patient and family.

It is the utmost importance to remind patients and guardians to prevent the cast from becoming wet. Many times the complications from a wet padding can be unnoticed and will not be discovered until the final follow-up when the cast is removed. In order to prevent further skin complications that can lead to significant infection and injury, educating the parents on signs of wound infection such as deterioration of the fiberglass or a strong malodor from the cast must be performed.

SKIN COMPLICATIONS

Skin complications from cast application is a common occurrence that can range from minor skin excoriations to severe pressure ulcers that can eventually require surgical debridement and coverage^[31]. There are only several studies published that focused solely on pediatric skin complications associated with casting^[12,31].

Many of the skin complications we have encountered in the clinic or emergency department were likely due to poor cast padding. In order to prevent pressure ulcers, it is important to be aware of the locations of the extremity that have notable protuberances (*i.e.*, fibular head, heel, femoral epicondyles, *etc.*). At these areas, more padding needs to be placed to prevent excessive pressure. Difazio *et al.*^[31] published a recent study on reducing the incidence of casted-related skin complications, more specifically heel pad ulcers.

Through adding extra padding at the heel area in addition to respective provider education, they decreased the incidence of casted-related skin complications from 17.1 per 1000 lower extremity casts to 6.8.

CAST REMOVAL

The use of cast saws have brought much attention in the orthopedic literature^[1-4,7,24,32,33]. These studies have focused mainly on the complications that come with using the saw. Although they are routinely advertised to patients and their families that it is only intended to cut the fiberglass and not the child's skin, cast saws can still result in thermal injuries and abrasions.

Shuler *et al.*^[4] recently evaluated factors that prevented excessive increase in temperatures when using a cast saw blade. What they found was significant was the amount of cast padding and the relationship with temperature. They recommended four layers, as opposed to two, when applying the padding. This adjustment helped decrease the temperature by 8.0 °C.

Killian *et al.*^[3] provided another study that evaluated multiple factors that contribute to thermal injuries from cast saw use. In this study they compared thickness of casts, dullness of blades, and experience of cast saw users. What they concluded was that frequent changes to cast blades, cast thickness to be less than 3/8 inch, and a heightened sense of awareness on the temperature of the blade during cast saw use were important clinical factors that can prevent thermal injuries. They included a tip on how to gauge cast-saw blade temperature which was that if the user is unable to hold the blade with two fingers for longer than 5 s the blade is too hot.

Several articles on cast saw complications have emphasized the importance of the user's experience^[2,3,7,32]. Just like any new procedure, it has been studied that an inexperienced user can cause significant harm to the child if not done correctly. Brubacher *et al.*^[32] developed a cast removal training simulation using a fracture model and experimenting it with various levels of orthopedic attendings and residents. As expected, the more experience surgeons resulted in lower mean peak temperatures after cast removal. What they also discovered was that the beginner and intermediate groups were able to achieve progressively decreasing mean temperatures after they experienced more trials with the simulator. In addition, the study displayed the potential benefits of using a simulation workshop to allow providers of all skill levels to develop experience and comfort when using a cast saw.

At our institution, we strictly emphasize the importance of cast saw use. Our cast-saw blades are routinely checked on a weekly basis and a "blade status/change log" is maintained by our orthopedic technicians.

Using a Saw Stop[©] protective strip (Figure 5) is another way to further protect the limb from the cast saw during removal. The strip is placed directly over the webil layer on the side that the cast saw will cut. The fiberglass is then layered on top of the protective strip



Figure 5 Saw Stop® protective strip (A and B). This protective strip is placed on top of the webril layer before applying the fiberglass cast roll. The strip provides a durable protective layer for the cast saw to cut over.

and the cast saw user is now able to cut through the fiber glass without risk of contacting the skin because of the added protection layer. They are crucial to use if the person removing the cast is unsure of the quality integrity or even the presence of soft roll beneath the cast material. Having a dedicated formal teaching session(s) in place and a practical exam is recommended prior to allowing practitioner in any medical setting use a cast saw to remove a cast in any patient.

PATIENT EDUCATION

Equally as important as all the factors above when applying a cast, is the detailed patient education on how patients and patient's family can maintain this cast. As common as cast application and maintenance is for orthopedic surgeons, it is easily forgotten on how novel this treatment is for the patient and their families. Thus, emphasizing the "do's and don'ts" of cast care is imperative on preventing complications.

DiPaola *et al.*^[34] designed a prospective study on documenting the incidence and etiology related to unplanned cast changes. What they discovered was that the major reason for unplanned cast changes wasn't because of the technique of the cast application but rather patient non-adherence to instructions or lack of education on maintaining it.

The importance of patient education must be emphasized. After each cast application, the practitioner should have a discussion with the child and family that touches on numerous factors on cast care maintenance that should include how to prevent cast from becoming wet, avoiding inserting objects into the cast and how to handle certain irritating symptoms such as itchiness. Patients are provided with an educational handout on how to best care for their cast and it is translated into their native language when necessary.

CONCLUSION

Casting was one of the first methods of fracture treatment and remains as one of the most common modes of treatment. Perfecting the art of casting

remains crucial in ensuring optimal patient outcomes and preventing significant healthcare expenses related to complications.

The ideal cast has a long list of factors that need to be considered to ensure a high quality of patient care. A good cast should immobilize the extremity, remain comfortable, and not cause complications. These factors include the type of cast material and how much padding to apply at certain areas of the extremity. Afterwards, educating the patient and family on how to prevent the cast from getting wet will assist in maintenance, comfort and anxiety. Finally, learning how to properly use a cast saw to prevent thermal injury are just a few notable aspects of providing an optimal cast experience.

REFERENCES

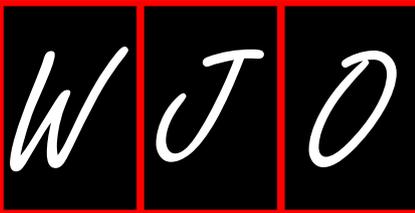
- 1 **Shore BJ**, Hutchinson S, Harris M, Bae DS, Kalish LA, Maxwell W, Waters P. Epidemiology and prevention of cast saw injuries: results of a quality improvement program at a single institution. *J Bone Joint Surg Am* 2014; **96**: e31 [PMID: 24553900 DOI: 10.2106/JBJS.L.01372]
- 2 **Puddy AC**, Sunkin JA, Aden JK, Walick KS, Hsu JR. Cast saw burns: evaluation of simple techniques for reducing the risk of thermal injury. *J Pediatr Orthop* 2014; **34**: e63-e66 [PMID: 25075891 DOI: 10.1097/BPO.0000000000000274]
- 3 **Killian JT**, White S, Lenning L. Cast-saw burns: comparison of technique versus material versus saws. *J Pediatr Orthop* 1999; **19**: 683-687 [PMID: 10488876 DOI: 10.1097/01241398-199909000-00026]
- 4 **Shuler FD**, Grisafi FN. Cast-saw burns: evaluation of skin, cast, and blade temperatures generated during cast removal. *J Bone Joint Surg Am* 2008; **90**: 2626-2630 [PMID: 19047707 DOI: 10.2106/JBJS.H.00119]
- 5 **Large TM**, Frick SL. Compartment syndrome of the leg after treatment of a femoral fracture with an early sitting spica cast. A report of two cases. *J Bone Joint Surg Am* 2003; **85-A**: 2207-2210 [PMID: 14630855]
- 6 **Roberts A**, Shaw KA, Boomsma SE, Cameron CD. Effect of Casting Material on the Cast Pressure After Sequential Cast Splitting. *J Pediatr Orthop* 2015: Epub ahead of print [PMID: 26090972 DOI: 10.1097/BPO.0000000000000574]
- 7 **Ansari MZ**, Swarup S, Ghani R, Tovey P. Oscillating saw injuries during removal of plaster. *Eur J Emerg Med* 1998; **5**: 37-39 [PMID: 10406417 DOI: 10.1097/00063110-199803000-00009]
- 8 **Weiss AP**, Schenck RC, Sponseller PD, Thompson JD. Peroneal nerve palsy after early cast application for femoral fractures in children. *J Pediatr Orthop* 1992; **12**: 25-28 [PMID: 1732291 DOI: 10.1097/01241398-199201000-00005]

- 9 **Mohler LR**, Pedowitz RA, Byrne TP, Gershuni DH. Pressure generation beneath a new thermoplastic cast. *Clin Orthop Relat Res* 1996; **(322)**: 262-267 [PMID: 8542703 DOI: 10.1097/00003086-199601000-00031]
- 10 **Garfin SR**, Mubarak SJ, Evans KL, Hargens AR, Akeson WH. Quantification of intracompartmental pressure and volume under plaster casts. *J Bone Joint Surg Am* 1981; **63**: 449-453 [PMID: 7204445]
- 11 **Mubarak SJ**, Frick S, Sink E, Rathjen K, Noonan KJ. Volkmann contracture and compartment syndromes after femur fractures in children treated with 90/90 spica casts. *J Pediatr Orthop* 2006; **26**: 567-572 [PMID: 16932092 DOI: 10.1097/01.bpo.0000230329.06460.f7]
- 12 **Wolff CR**, James P. The prevention of skin excoriation under children's hip spica casts using the goretex pantaloons. *J Pediatr Orthop* 1995; **15**: 386-388 [PMID: 7790500 DOI: 10.1097/01241398-199505000-00024]
- 13 **Fernandez DL**. Closed manipulation and casting of distal radius fractures. *Hand Clin* 2005; **21**: 307-316 [PMID: 16039442 DOI: 10.1016/j.hcl.2005.02.004]
- 14 **Webb GR**, Galpin RD, Armstrong DG. Comparison of short and long arm plaster casts for displaced fractures in the distal third of the forearm in children. *J Bone Joint Surg Am* 2006; **88**: 9-17 [PMID: 16391244 DOI: 10.2106/JBJS.E.00131]
- 15 **Ferguson J**, Nicol RO. Early spica treatment of pediatric femoral shaft fractures. *J Pediatr Orthop* 2000; **20**: 189-192 [PMID: 10739280 DOI: 10.1097/01241398-200003000-00011]
- 16 **Illgen R**, Rodgers WB, Hresko MT, Waters PM, Zurakowski D, Kasser JR. Femur fractures in children: treatment with early sitting spica casting. *J Pediatr Orthop* 1998; **18**: 481-487 [PMID: 9661858 DOI: 10.1097/01241398-199807000-00016]
- 17 **Sawyer JR**, Ivie CB, Huff AL, Wheeler C, Kelly DM, Beaty JH, Canale ST. Emergency room visits by pediatric fracture patients treated with cast immobilization. *J Pediatr Orthop* 2010; **30**: 248-252 [PMID: 20357591 DOI: 10.1097/BPO.0b013e3181d213bc]
- 18 **Newton PO**, Mubarak SJ. Financial aspects of femoral shaft fracture treatment in children and adolescents. *J Pediatr Orthop* 1994; **14**: 508-512 [PMID: 8077437 DOI: 10.1097/01241398-199407000-00017]
- 19 **Halanski M**, Noonan KJ. Cast and splint immobilization: complications. *J Am Acad Orthop Surg* 2008; **16**: 30-40 [PMID: 18180390 DOI: 10.5435/00124635-200801000-00005]
- 20 **Iltar S**, Alemdaroğlu KB, Say F, Aydoğan NH. The value of the three-point index in predicting redisplacement of diaphyseal fractures of the forearm in children. *Bone Joint J* 2013; **95-B**: 563-567 [PMID: 23539712 DOI: 10.1302/0301-620X.95B4.31143]
- 21 **Kamat AS**, Pierse N, Devane P, Mutimer J, Horne G. Redefining the cast index: the optimum technique to reduce redisplacement in pediatric distal forearm fractures. *J Pediatr Orthop* 2012; **32**: 787-791 [PMID: 23147621 DOI: 10.1097/BPO.0b013e318272474d]
- 22 **Chess DG**, Hyndman JC, Leahey JL, Brown DC, Sinclair AM. Short arm plaster cast for distal pediatric forearm fractures. *J Pediatr Orthop* 1994; **14**: 211-213 [PMID: 8188836 DOI: 10.1097/01241398-199403000-00015]
- 23 **Edmonds EW**, Capelo RM, Stearns P, Bastrom TP, Wallace CD, Newton PO. Predicting initial treatment failure of fiberglass casts in pediatric distal radius fractures: utility of the second metacarpal-radius angle. *J Child Orthop* 2009; **3**: 375-381 [PMID: 19701659 DOI: 10.1007/s11832-009-0198-1]
- 24 **Zaino CJ**, Patel MR, Arief MS, Pivec R. The effectiveness of bivalving, cast spreading, and webril cutting to reduce cast pressure in a fiberglass short arm cast. *J Bone Joint Surg Am* 2015; **97**: 374-380 [PMID: 25740027 DOI: 10.2106/JBJS.N.00579]
- 25 **Robert CE**, Jiang JJ, Khoury JG. A prospective study on the effectiveness of cotton versus waterproof cast padding in maintaining the reduction of pediatric distal forearm fractures. *J Pediatr Orthop* 2011; **31**: 144-149 [PMID: 21307707 DOI: 10.1097/BPO.0b013e318209d83a]
- 26 **Kleis K**, Schlechter JA, Doan A, Farnsworth CL, Edmonds EW. Under Pressure: The Utility of Splitting Fiberglass Casts. Orthopedic Trauma Association, 2015
- 27 **Gannaway JK**, Hunter JR. Thermal effects of casting materials. *Clin Orthop Relat Res* 1983; **(181)**: 191-195 [PMID: 6641053 DOI: 10.1097/00003086-198312000-00031]
- 28 **Lavalette R**, Pope MH, Dickstein H. Setting temperatures of plaster casts. The influence of technical variables. *J Bone Joint Surg Am* 1982; **64**: 907-911 [PMID: 7085719]
- 29 **Berman AT**, Parks BG. A comparison of the mechanical properties of fiberglass cast materials and their clinical relevance. *J Orthop Trauma* 1990; **4**: 85-92 [PMID: 2313436]
- 30 **McDowell M**, Nguyen S, Schlechter J. A Comparison of Various Contemporary Methods to Prevent a Wet Cast. *J Bone Joint Surg Am* 2014; **96**: e99 [PMID: 24951750 DOI: 10.2106/JBJS.M.00203]
- 31 **Difazio RL**, Harris M, Feldman L, Mahan ST. Reducing the Incidence of Cast-related Skin Complications in Children Treated With Cast Immobilization. *J Pediatr Orthop* 2015: Epub ahead of print [PMID: 26683501 DOI: 10.1097/BPO.0000000000000713]
- 32 **Brubacher JW**, Karg J, Weinstock P, Bae DS. A Novel Cast Removal Training Simulation to Improve Patient Safety. *J Surg Educ* 2016; **73**: 7-11 [PMID: 26385318 DOI: 10.1016/j.jsurg.2015.08.004]
- 33 **Nielsen DM**, Ricketts DM. Where to split plaster casts. *Injury* 2005; **36**: 588-589 [PMID: 15826615 DOI: 10.1016/j.injury.2004.11.021]
- 34 **DiPaola MJ**, Abzug JM, Pizzutillo PD, Herman MJ. Incidence and etiology of unplanned cast changes for fractures in the pediatric population. *J Pediatr Orthop* 2014; **34**: 643-646 [PMID: 24787307 DOI: 10.1097/BPO.0000000000000191]

P- Reviewer: Emara K, Matuszewski LS, Vulcano E

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D





Implant retention after acute and hematogenous periprosthetic hip and knee infections: Whom, when and how?

Georgios K Triantafyllopoulos, Vasileios Soranoglou, Stavros G Memtsoudis, Lazaros A Poultsides

Georgios K Triantafyllopoulos, Vasileios Soranoglou, Lazaros A Poultsides, Department of Orthopaedic Surgery, Division of Adult Reconstruction and Joint Replacement, Hospital for Special Surgery, Weill Medical College of Cornell University, New York, NY 10021, United States

Stavros G Memtsoudis, Department of Anesthesiology, Hospital for Special Surgery, Weill Medical College of Cornell University, New York, NY 10021, United States

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: The authors have no potential conflicts of interest to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Lazaros A Poultsides, MD, MSc, PhD, Department of Orthopaedic Surgery, Division of Adult Reconstruction and Joint Replacement, Hospital for Special Surgery, Weill Medical College of Cornell University, 535 East 70th Street, New York, NY 10021, United States. poultsidesl@hss.edu
Telephone: +1-212-7742387
Fax: +1-646-7978939

Received: April 25, 2016
Peer-review started: April 26, 2016
First decision: June 16, 2016
Revised: June 23, 2016
Accepted: July 11, 2016

Article in press: July 13, 2016
Published online: September 18, 2016

Abstract

Periprosthetic joint infections (PJI) of the hip and the knee are grossly classified as early post-operative, acute hematogenous and late chronic infections. Whereas two-stage exchange arthroplasty is the standard of care in North America for treating chronic infections, irrigation and debridement (I and D) with retention of implants has been used in an attempt to treat the other two types of PJIs. The rationale of this approach is that a PJI may be eradicated without the need of explanting the prostheses, as long as it has not transitioned into a chronic state. With the present paper, we review current evidence regarding the role of I and D with implant retention for treating PJIs of the hip and the knee. While a very wide range of success rates is reported in different studies, a short period of time between initiation of symptoms and intervention seems to play a prominent role with regards to a successful outcome. Moreover, pathogens of higher virulence and resistance to antibiotics are associated with a poorer result. Specific comorbidities have been also correlated with a less favorable outcome. Finally, one should proceed with serial I and Ds only under the condition that a pre-defined, aggressive protocol is applied. In conclusion, when treating a PJI of the hip or the knee, all the above factors should be considered in order to decide whether the patient is likely to benefit from this approach.

Key words: Irrigation and debridement; Periprosthetic infection; Total knee arthroplasty; Implant retention; Total hip arthroplasty

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: An infected total joint arthroplasty represents a significant burden to patients, as well as to orthopaedic surgeons. Previously, irrigation and debridement with retention of implants has been advocated for certain types of periprosthetic infections. The purpose of the present paper is to review the indications, success rates and factors determining the outcome of this treatment option for periprosthetic infections of the hip and the knee.

Triantafyllopoulos GK, Soranoglou V, Memtsoudis SG, Poultsides LA. Implant retention after acute and hematogenous periprosthetic hip and knee infections: Whom, when and how? *World J Orthop* 2016; 7(9): 546-552 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/546.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.546>

INTRODUCTION

Periprosthetic hip and knee infections: Trends, diagnosis, classification and treatment

Total joint arthroplasty (TJA) is a very useful tool in the hands of orthopaedic surgeons, as it can relieve symptoms and significantly improve the quality of life in patients with end-stage arthritis of the hip and the knee. In the past decades, the use of this modality has known a remarkable growth, which is expected to continue in the future. For example, by the year 2020 the estimated annual number of total hip arthroplasties (THAs) will exceed 500000 procedures^[1]. On the other hand, this will also lead to an increase in complications related with TJA, among which periprosthetic joint infection (PJI) is one of the most devastating for the patient. In spite of preventive measures available, the incidence of PJI remains substantial as it ranges from 1% to 3% after primary TJA^[2-5], and can be 4 times greater after revision TJA^[6].

Implant colonization may occur with either intraoperative contamination, spreading from an adjacent infectious site or hematogenous seeding from a distant site^[7], with coagulase-negative staphylococci and *Staphylococcus aureus* species being the most dominant pathogens^[8-11]. Diagnosis can be easily made when obvious sequelae of infection are present, such as a draining sinus. However, in many cases such signs are absent and a complex diagnostic evaluation is needed. No single method provides 100% diagnostic specificity and sensitivity. The Musculoskeletal Infection Society introduced specific criteria for the diagnosis of a PJI^[12]. The combination of different modalities significantly increase sensitivity and specificity for diagnosing PJI^[13,14]. Moreover, synovial biomarkers, including alpha-defensin and leukocyte esterase, have been proven accurate diagnostic tools for PJI with high sensitivity and specificity^[15]. Nonetheless, sophisticated methods are expensive and not widely available, and therefore cannot be recommended for routine use.

PJIs of the hip are classified into four types, as proposed by Tsukayama *et al.*^[16]. Type I includes positive intraoperative cultures in patients undergoing revision surgery for non-infectious etiology; Type II represents early infections developing within one month postoperatively; late infections presenting within more than one month postoperatively are characterized as Type III infections; finally, Type IV infections are of acute hematogenous nature and are correlated with an identifiable event leading to bacteremia. A similar system has been introduced for PJIs of the knee^[17]: Type I includes positive intraoperative cultures obtained during a revision surgery for a cause other than infection; Type II PJIs are early infections presenting within 4 wk after surgery and include Types II A (superficial) and II B (deep); acute hematogenous deep infections with an onset of more than 4 wk postoperatively are classified as Type III infections; lastly, Type IV PJIs of the knee are late deep infections developing after 4 wk since the index procedure.

The standard of treatment for PJI is a combination of surgical interventions with the goal of reducing microbial load and administration of antibiotics. Two-stage revision is considered to be the gold standard for management of late chronic PJIs in North America^[18]. On the other hand, eradicating infection with retention of the prosthesis when possible may be associated with superior functional outcomes. Irrigation and debridement (I and D) with exchange of prosthetic modular parts has been long used with respect to that goal. The purpose of the present paper is to review the indications, success rates and risk factors that determine the outcome of I and D for PJIs of the hip and the knee.

I AND D: PROCEDURE DESCRIPTION

The patient should be off any antibiotics for at least 5 d before the procedure. The affected limb is prepped and draped, the previously healed incision is used and the affected joint is adequately exposed (Figure 1A). A total number of six tissue samples should be obtained and sent for cultures and sensitivity testing. Next, the modular parts, including femoral head and polyethylene liner for a THA and the polyethylene liner for TKA, are removed to gain access to all aspects of the joint and a thorough debridement is performed. All grossly infected and necrotic soft-tissues are meticulously excised (Figure 1B). Great care should be taken to circumferentially debride the articular capsule in both the hip and the knee. After the joint is debrided to macroscopically healthy tissues, the joint is copiously irrigated with antibiotic containing saline. Modular parts are exchanged and the wound is closed. It should be noted that even though exchange of modular parts is advised^[18], it may not be always feasible, especially in settings where implant availability is limited. There is no consensus on the duration of intravenous antibiotics administration after the procedure^[19]. A common approach is to place the patient on a 6 wk treatment with

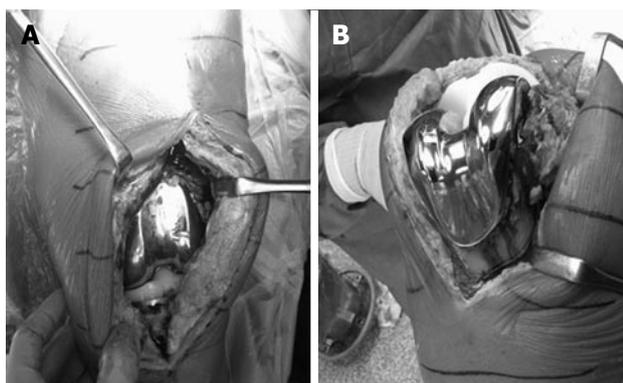


Figure 1 Irrigation and debridement for an infected total knee arthroplasty with retention of implants. A: The joint is exposed through the previously healed incision; B: Note the extensile debridement of the synovium on the anterior aspect of the femur. Debridement of the infected tissues should be carried out throughout the joint, including the posterior capsule.

antibiotics (two weeks of intravenously administered antibiotics followed by another 4 wk of p.o. antibiotics), based on culture and sensitivity results.

The technique described above is the open technique with exchange of modular parts. In the previous years, there was a trend towards performing I and D arthroscopically, especially for periprosthetic infections of the knee^[20,21]. However, recently there has been a recommendation against this approach, as it does not allow access to all aspects of the joint and therefore the debridement may be suboptimal^[22].

INDICATIONS

Previously, Del Pozo *et al.*^[23] have outlined the indications of I and D for treating PJIs. According to the authors, these include an infected prosthesis that was implanted within less than 3 mo or a hematogenous infection, with duration of symptoms of less than 3 wk, absence of sinus tract or abscess, stability of implants and a pathogen other than multi-drug resistant microorganisms, Enterococcus species, quinolone-resistant *Pseudomonas* and fungi.

Recently, the participants of a consensus meeting on periprosthetic infections strongly agreed that I and D may be a viable alternative for patients with early infections that develop within 3 mo post index procedure, as well as with late hematogenous infections; symptoms should have a duration of less than 3 wk^[19]. Eradicating infection while avoiding removal of the prostheses may allow for lower morbidity and better function. Published series of patients treated with I and D for PJI of the hip and the knee show great variability in methodology, success rates and identified prognostic factors with regards to outcome.

WHAT IS THE EVIDENCE?

I and D for PJI of the Hip

Implant retention with I and D of the hip for a Type II

or IV PJI has been previously reported to be 70% in a previous large series^[24]. Westberg *et al.*^[25] have reported a 71% success rate of I and D in early hip PJIs. In the series of Tsukayama *et al.*^[16], retention of implants was attained in 70.3% of cases. Barberán *et al.*^[26] had a success rate of 71.9%, and Vilchez *et al.*^[27] reported that I and D successfully treated infection with implant retention in 75.5% of patients. On the other hand, other authors have published greatly variable results, with success rates ranging from 14% to 100%^[21,28-46] (Table 1).

Symptom duration is a significant factor predicting the outcome of I and D of the hip. When a cut-off point of 5 d of symptom duration was used, it was noted that patients with symptoms of more than 5 d had 95.2% lower odds of success compared to patients with shorter duration of symptoms^[24]. Similarly, Sukeik *et al.*^[36] found that performing I and D more than 5 d after the onset of symptoms led to less favorable outcomes. Others have proposed an even prompt intervention, in as shortly as within 2 d from symptom onset^[30]. In other studies, the suggested duration of symptoms within which such an intervention is more probable to be successful ranges from one to four weeks^[40,42,45]. Despite this variability, we may conclude that once the diagnosis of a type II or IV PJI of the hip is established, action should be prompt from the part of the surgeon when the goal is to retain the implants. The decrease in the probability of successful I and D has been calculated to be 17.7% for each additional day of delay in treatment^[24]. A greater duration of symptoms allows formation of the biofilm layer, which provides protection against immune response and resistance against antibiotics. Once this biofilm is formed, I and D with implant retention is less probable to control the infection^[43].

The type of pathogen also plays a role in the outcomes of I and D of the hip. Patients with methicillin-resistant staphylococci have been correlated with worse outcomes^[24]. Barberán *et al.*^[26] also reported worse outcomes in patients infected with methicillin-resistant *Staphylococcus aureus* (MRSA). In addition, infections with MRSA, methicillin-resistant *Staphylococcus epidermidis* and vancomycin-resistant Enterococci have been associated with inferior success rates after I and D^[40]. Staphylococcal infections have been identified as a negative prognostic factor by other investigators as well^[21,29,31,41,42]. In cases of infections with multi-drug resistant pathogens, a more aggressive treatment strategy is warranted and even exchange arthroplasty (either in one or two stages) may be considered.

Other factors that have been found to predict outcomes of I and D of the hip include obesity^[24], ASA score and purulence^[29], a history of previous infection^[40] and elevated inflammatory markers^[27,34,40,42]. These factors are associated either with host's impaired immune system response to infection, or with severity of infections and should be considered for decision-making. Additionally, patients with one or more local or systemic compromises according to the Cierny classification have been also correlated with inferior outcomes after I and D for a PJI

Table 1 Reported success rates of irrigation and debridement for treating periprosthetic infections of the hip and the knee

Ref.	Patients	Success rate for PJI of the hip	Success rate for PJI of the knee	Cumulative success rate
Aboltins <i>et al.</i> ^[28]	13	92%	85.70%	90%
Azzam <i>et al.</i> ^[29]	53	47.83%	45.30%	44.60%
Barberán <i>et al.</i> ^[26]	32	71.90%	57.20%	65%
Bradbury <i>et al.</i> ^[52]	19	-	16%	-
Brandt <i>et al.</i> ^[30]	7	28.60%	38.50%	36.40%
Buller <i>et al.</i> ^[40]	62	56.50%	50.60%	51.80%
Burger <i>et al.</i> ^[49]	39	-	17.90%	-
Byren <i>et al.</i> ^[21]	52	86.50%	74.50%	80.60%
Chiu <i>et al.</i> ^[51]	40	-	30%	-
Choi <i>et al.</i> ^[31]	92	50%	-	-
Choong <i>et al.</i> ^[32]	14	78.60%	-	-
Cierny <i>et al.</i> ^[48]	43	-	-	66%
Crockarell <i>et al.</i> ^[44]	42	14%	-	-
Engesæter <i>et al.</i> ^[46]	180	76%	-	-
Estes <i>et al.</i> ^[57]	20	100%	87.50%	90%
Fehring <i>et al.</i> ^[43]	86	37.50%	37%	37.20%
Gardner <i>et al.</i> ^[50]	44	-	43.20%	-
Geurts <i>et al.</i> ^[45]	69	82.60%	85%	83.10%
Klouche <i>et al.</i> ^[63]	12	75%	-	-
Konigsberg <i>et al.</i> ^[33]	20	80%	77.30%	78.50%
Koyonos <i>et al.</i> ^[41]	60	30%	38.50%	35%
Kuiper <i>et al.</i> ^[42]	62	61.30%	75.90%	66%
Marculescu <i>et al.</i> ^[56]	91	-	-	60%
Martel-Lafarriere <i>et al.</i> ^[59]	34	-	-	60%
Martínez-Pastor <i>et al.</i> ^[34]	15	73.30%	75%	74.50%
Meehan <i>et al.</i> ^[35]	19	66.70%	100%	89.55%
Mont <i>et al.</i> ^[53]	24	-	83.30%	-
Peel <i>et al.</i> ^[60]	43	71.40%	93%	79.10%
Rasouli <i>et al.</i> ^[38]	10	83.30%	0%	50%
Segawa <i>et al.</i> ^[55]	28	-	78%	-
Sukeik <i>et al.</i> ^[36]	26	77%	-	-
Tattevin <i>et al.</i> ^[57]	69	-	-	38.20%
Teeny <i>et al.</i> ^[54]	21	-	29%	-
Triantafyllopoulos <i>et al.</i> ^[47]	78	-	55.10%	-
Triantafyllopoulos <i>et al.</i> ^[24]	60	70%	-	-
Tsukayama <i>et al.</i> ^[16]	106	70.30%	-	-
Van Kleunen <i>et al.</i> ^[61]	13	-	-	61.50%
Vilchez <i>et al.</i> ^[27]	18	88.90%	68.60%	75.50%
Westberg <i>et al.</i> ^[25]	38	71%	-	-
Zürcher-Pfund <i>et al.</i> ^[20]	21	-	33%	-

PJI: Periprosthetic joint infection.

of the hip^[48].

I and D for PJI of the knee

Buller *et al.*^[40], in their large series of 247 patients with PJI of the knee, reported a success rate of 50.6% for I and D. Similarly, in a series of 78 patients with PJI of the knee treated with I and D, the success rate was found to be 56.3%^[47]. A higher success rate (74.5%) was reported by Byren *et al.*^[21] among 51 patients with PJI of the knee. In contrast, in the study of Koyonos *et al.*^[41], I and D was successful in only 38.5%. In the literature, there are studies with highly variable success rates, that range from 16% to 100%^[20,26-30,33-35,37,42,43,45,49-55] (Table 1). These studies, however, show significant methodological inconsistencies.

Similarly to the hips, duration of symptoms is also identified as a factor predicting the outcomes of I and D. In studies where PJIs of both the hip and the knee were included, favorable outcomes were reported when the

intervention was undertaken within an interval ranging from 1-4 wk^[40,42,45,56]. In other reports, the suggested timing for a successful outcome is within 5 d since symptom onset^[47,57]. Others have proposed an even lower cut-off point of 2 d^[30]. For each additional day that treatment delays, a 7.5% decrease in the odds of success has been calculated^[47]. This highlights the importance of timely intervention, as the gradual formation of the protective biofilm may prevent eventual eradication of the pathogen without removal of the prosthesis.

The type of pathogen also predicts outcomes of I and D in the setting of a PJI of the knee. As is the case for the hip, MRSA infections have been associated with poorer outcomes^[26,40,47]. Treatment failure has been correlated with staphylococcal infections in several previous reports^[21,29,33,41,56]. This may be explained by the higher microorganism virulence^[58], the formation of biofilm and the increased rates of resistance to antibiotics that characterize staphylococcal strains.

For PJI of the knee, ASA score and joint purulence^[29,56,59], preoperative levels of inflammatory markers^[34,40,42], and prior infection^[40] have been also identified as factors affecting outcomes of I and D. In contrast to the hip, revision surgery^[21], as well as thyroid disease^[47], has been reported as additional prognostic factors for I and D of a knee PJI.

The role of serial I and Ds

In a previous consensus meeting, the participants recommended against performing serial I and Ds, unless this approach is included in a specific protocol^[22]. Studies utilizing a predefined protocol of serial interventions exhibit high success rates. When gentamycin-loaded cement beads were used in combination with a repeat I and D after 2 wk, infection control was established in 83.1% of patients^[45]. Kuiper *et al.*^[42] used a similar protocol, with a success rate of 66.1%. A more aggressive approach was adopted by Peel *et al.*^[60], which included three I and Ds within 7-10 d; the authors reported an 86% success rate. Estes *et al.*^[37] performed 2 I and Ds 7 d apart using antibiotic-loaded cement beads and reported a 90% success rate. With a protocol consisting at least 2 I and Ds within 2-3 d, Choong *et al.*^[32] reported successful outcomes in 78.6% of patients. On the other hand, in studies where no particular protocol for performing serial I and Ds is followed, the results have been more variable and range from 25% to 100%^[20,21,25,27-29,31,36,53,61,62].

Time is still a significant factor when the approach of serial I and Ds is chosen. It has been shown that performing a subsequent I and D within more than 20 d after the first procedure is associated with 97.4% lower odds of implant retention^[62]. Specific protocols with serial I and Ds involve performing the subsequent procedure in no more than 14 d and, as already described, were associated with superior results. Again, longer duration of symptoms has been also associated with failure of multiple I and Ds^[62] as it allows for biofilm formation and transition to infection chronicity, as previously described.

Serial I and Ds have been found less likely to be of success in PJIs of the knee than in hip infections^[62]. This may be attributed to differences with regards to the soft-tissue envelope of each joint, as well as to vascular supply. In the same study, patients treated with multiple I and Ds were more likely to have vascular disease^[62]. These findings, however, have not been reproduced by other reports and therefore further investigation is needed in order to elucidate their potential impact.

CONCLUSION

I and D with the goal of implant retention is still an important tool in the armamentarium of the orthopaedic surgeon for early postoperative and late acute hematogenous PJIs. In such cases, intervention should be timely and aggressive, as each additional day lowers the odds for a successful outcome. Furthermore, the ideal candidate should have an infection with a low-virulence

pathogen and be without comorbidities that have been associated with a less favorable result. Finally, after one failed I and D, the surgeon should be very cautious about repeating the procedure, unless a structured and aggressive protocol incorporating serial I and Ds within a short time interval is applied.

REFERENCES

- 1 Kurtz SM, Ong KL, Lau E, Bozic KJ. Impact of the economic downturn on total joint replacement demand in the United States: updated projections to 2021. *J Bone Joint Surg Am* 2014; **96**: 624-630 [PMID: 24740658 DOI: 10.2106/JBJS.M.00285]
- 2 Salvati EA, González Della Valle A, Masri BA, Duncan CP. The infected total hip arthroplasty. *Instr Course Lect* 2003; **52**: 223-245 [PMID: 12690851]
- 3 Hanssen AD, Rand JA. Evaluation and treatment of infection at the site of a total hip or knee arthroplasty. *Instr Course Lect* 1999; **48**: 111-122 [PMID: 10098033]
- 4 Phillips JE, Crane TP, Noy M, Elliott TS, Grimer RJ. The incidence of deep prosthetic infections in a specialist orthopaedic hospital: a 15-year prospective survey. *J Bone Joint Surg Br* 2006; **88**: 943-948 [PMID: 16799001]
- 5 Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. *Clin Orthop Relat Res* 2001; **(392)**: 15-23 [PMID: 11716377 DOI: 10.1097/00003086-200111000-00003]
- 6 Mortazavi SM, Molligan J, Austin MS, Purtill JJ, Hozack WJ, Parvizi J. Failure following revision total knee arthroplasty: infection is the major cause. *Int Orthop* 2011; **35**: 1157-1164 [PMID: 20959981 DOI: 10.1007/s00264-010-1134-1]
- 7 Zimmerli W, Ochsner PE. Management of infection associated with prosthetic joints. *Infection* 2003; **31**: 99-108 [PMID: 12682815 DOI: 10.1007/s15010-002-3079-9]
- 8 Bjerke-Kroll BT, Christ AB, McLawhorn AS, Sculco PK, Jules-Elysée KM, Sculco TP. Periprosthetic joint infections treated with two-stage revision over 14 years: an evolving microbiology profile. *J Arthroplasty* 2014; **29**: 877-882 [PMID: 24199997 DOI: 10.1016/j.arth.2013.09.053]
- 9 Stefánsdóttir A, Johansson D, Knutson K, Lidgren L, Robertsson O. Microbiology of the infected knee arthroplasty: report from the Swedish Knee Arthroplasty Register on 426 surgically revised cases. *Scand J Infect Dis* 2009; **41**: 831-840 [PMID: 19922065 DOI: 10.3109/00365540903186207]
- 10 Nickinson RS, Board TN, Gambhir AK, Porter ML, Kay PR. The microbiology of the infected knee arthroplasty. *Int Orthop* 2010; **34**: 505-510 [PMID: 19458950 DOI: 10.1007/s00264-009-0797-y]
- 11 Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL. Guiding empirical antibiotic therapy in orthopaedics: The microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. *J Infect* 2007; **55**: 1-7 [PMID: 17343916 DOI: 10.1016/j.jinf.2007.01.007]
- 12 Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, Garvin KL, Mont MA, Wongworawat MD, Zalavras CG. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res* 2011; **469**: 2992-2994 [PMID: 21938532 DOI: 10.1007/s11999-011-2102-9]
- 13 Kwee TC, Kwee RM, Alavi A. FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis. *Eur J Nucl Med Mol Imaging* 2008; **35**: 2122-2132 [PMID: 18704405 DOI: 10.1007/s00259-008-0887-x]
- 14 Gemmel F, Van den Wyngaert H, Love C, Welling MM, Gemmel P, Palestro CJ. Prosthetic joint infections: radionuclide state-of-the-art imaging. *Eur J Nucl Med Mol Imaging* 2012; **39**: 892-909 [PMID: 22361912 DOI: 10.1007/s00259-012-2062-7]
- 15 Wyatt MC, Beswick AD, Kunutsor SK, Wilson MJ, Whitehouse MR, Blom AW. The Alpha-Defensin Immunoassay and Leukocyte Esterase Colorimetric Strip Test for the Diagnosis of Periprosthetic

- Infection: A Systematic Review and Meta-Analysis. *J Bone Joint Surg Am* 2016; **98**: 992-1000 [PMID: 27307359 DOI: 10.2106/JBJS.15.01142]
- 16 **Tsukayama DT**, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. *J Bone Joint Surg Am* 1996; **78**: 512-523 [PMID: 8609130]
 - 17 **Tsukayama DT**, Goldberg VM, Kyle R. Diagnosis and management of infection after total knee arthroplasty. *J Bone Joint Surg Am* 2003; **85-A** Suppl 1: S75-S80 [PMID: 12540674]
 - 18 **Windsor RE**. Management of total knee arthroplasty infection. *Orthop Clin North Am* 1991; **22**: 531-538 [PMID: 1852429]
 - 19 **Haasper C**, Buttaro M, Hozack W, Aboltins CA, Borens O, Callaghan JJ, de Carvalho PI, Chang Y, Corona P, Da Rin F, Esposito S, Fehring TK, Sanchez XF, Lee GC, Martinez-Pastor JC, Mortazavi SM, Noiseux NO, Peng KT, Schutte HD, Schweitzer D, Trebše R, Tsiridis E, Whiteside L. Irrigation and debridement. *J Arthroplasty* 2014; **29**: 100-103 [PMID: 24360491 DOI: 10.1016/j.arth.2013.09.043]
 - 20 **Zürcher-Pfund L**, Uçkay I, Legout L, Gamulin A, Vaudaux P, Peter R. Pathogen-driven decision for implant retention in the management of infected total knee prostheses. *Int Orthop* 2013; **37**: 1471-1475 [PMID: 23695880 DOI: 10.1007/s00264-013-1923-4]
 - 21 **Byren I**, Bejon P, Atkins BL, Angus B, Masters S, McLardy-Smith P, Gundle R, Berend A. One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome. *J Antimicrob Chemother* 2009; **63**: 1264-1271 [PMID: 19336454 DOI: 10.1093/jac/dkp107]
 - 22 **Parvizi J**, Gehrke T, Chen AF. Proceedings of the International Consensus on Periprosthetic Joint Infection. *Bone Joint J* 2013; **95-B**: 1450-1452 [PMID: 24151261 DOI: 10.1302/0301-620X.95.B11.33135]
 - 23 **Del Pozo JL**, Patel R. Clinical practice. Infection associated with prosthetic joints. *N Engl J Med* 2009; **361**: 787-794 [PMID: 19692690 DOI: 10.1056/NEJMc0905029]
 - 24 **Triantafyllopoulos GK**, Poultsides LA, Sakellariou VI, Zhang W, Sculco PK, Ma Y, Sculco TP. Irrigation and debridement for periprosthetic infections of the hip and factors determining outcome. *Int Orthop* 2015; **39**: 1203-1209 [PMID: 25820839 DOI: 10.1007/s00264-015-2753-3]
 - 25 **Westberg M**, Grøgaard B, Snorrason F. Early prosthetic joint infections treated with debridement and implant retention: 38 primary hip arthroplasties prospectively recorded and followed for median 4 years. *Acta Orthop* 2012; **83**: 227-232 [PMID: 22489892 DOI: 10.3109/17453674.2012.678801]
 - 26 **Barberán J**, Aguilar L, Carroquino G, Giménez MJ, Sánchez B, Martínez D, Prieto J. Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. *Am J Med* 2006; **119**: 993.e7-993.10 [PMID: 17071171 DOI: 10.1016/j.amjmed.2006.03.036]
 - 27 **Vilchez F**, Martínez-Pastor JC, García-Ramiro S, Bori G, Maculé F, Sierra J, Font L, Mensa J, Soriano A. Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to *Staphylococcus aureus* treated with debridement. *Clin Microbiol Infect* 2011; **17**: 439-444 [PMID: 20412187 DOI: 10.1111/j.1469-0691.2010.03244.x]
 - 28 **Aboltins CA**, Page MA, Buising KL, Jenney AW, Daffy JR, Choong PF, Stanley PA. Treatment of staphylococcal prosthetic joint infections with debridement, prosthesis retention and oral rifampicin and fusidic acid. *Clin Microbiol Infect* 2007; **13**: 586-591 [PMID: 17331125 DOI: 10.1111/j.1469-0691.2007.01691.x]
 - 29 **Azzam KA**, Seeley M, Ghanem E, Austin MS, Purtill JJ, Parvizi J. Irrigation and debridement in the management of prosthetic joint infection: traditional indications revisited. *J Arthroplasty* 2010; **25**: 1022-1027 [PMID: 20378306 DOI: 10.1016/j.arth.2010.01.104]
 - 30 **Brandt CM**, Sistrunk WW, Duffy MC, Hanssen AD, Steckelberg JM, Ilstrup DM, Osmon DR. *Staphylococcus aureus* prosthetic joint infection treated with debridement and prosthesis retention. *Clin Infect Dis* 1997; **24**: 914-919 [PMID: 9142792 DOI: 10.1093/clinids/24.5.914]
 - 31 **Choi HR**, von Knoch F, Kandil AO, Zurakowski D, Moore S, Malchau H. Retention treatment after periprosthetic total hip arthroplasty infection. *Int Orthop* 2012; **36**: 723-729 [PMID: 21792609 DOI: 10.1007/s00264-011-1324-5]
 - 32 **Choong PF**, Dowsey MM, Carr D, Daffy J, Stanley P. Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampin-based regimen. *Acta Orthop* 2007; **78**: 755-765 [PMID: 18236181 DOI: 10.1080/17453670710014527]
 - 33 **Konigsberg BS**, Della Valle CJ, Ting NT, Qiu F, Sporer SM. Acute hematogenous infection following total hip and knee arthroplasty. *J Arthroplasty* 2014; **29**: 469-472 [PMID: 23998990 DOI: 10.1016/j.arth.2013.07.021]
 - 34 **Martínez-Pastor JC**, Muñoz-Mahamad E, Vilchez F, García-Ramiro S, Bori G, Sierra J, Martínez JA, Font L, Mensa J, Soriano A. Outcome of acute prosthetic joint infections due to gram-negative bacilli treated with open debridement and retention of the prosthesis. *Antimicrob Agents Chemother* 2009; **53**: 4772-4777 [PMID: 19687237 DOI: 10.1128/AAC.00188-09]
 - 35 **Meehan AM**, Osmon DR, Duffy MC, Hanssen AD, Keating MR. Outcome of penicillin-susceptible streptococcal prosthetic joint infection treated with debridement and retention of the prosthesis. *Clin Infect Dis* 2003; **36**: 845-849 [PMID: 12652384 DOI: 10.1086/368182]
 - 36 **Sukeik M**, Patel S, Haddad FS. Aggressive early débridement for treatment of acutely infected cemented total hip arthroplasty. *Clin Orthop Relat Res* 2012; **470**: 3164-3170 [PMID: 22826016 DOI: 10.1007/s11999-012-2500-7]
 - 37 **Estes CS**, Beauchamp CP, Clarke HD, Spangehl MJ. A two-stage retention débridement protocol for acute periprosthetic joint infections. *Clin Orthop Relat Res* 2010; **468**: 2029-2038 [PMID: 20224958 DOI: 10.1007/s11999-010-1293-9]
 - 38 **Rasouli MR**, Tripathi MS, Kenyon R, Wetters N, Della Valle CJ, Parvizi J. Low rate of infection control in enterococcal periprosthetic joint infections. *Clin Orthop Relat Res* 2012; **470**: 2708-2716 [PMID: 22552769 DOI: 10.1007/s11999-012-2374-8]
 - 39 **Klouches S**, Leonard P, Zeller V, Lhotellier L, Graff W, Leclerc P, Mamoudy P, Sariali E. Infected total hip arthroplasty revision: one- or two-stage procedure? *Orthop Traumatol Surg Res* 2012; **98**: 144-150 [PMID: 22364829 DOI: 10.1016/j.otsr.2011.08.018]
 - 40 **Buller LT**, Sabry FY, Easton RW, Klika AK, Barsoum WK. The preoperative prediction of success following irrigation and debridement with polyethylene exchange for hip and knee prosthetic joint infections. *J Arthroplasty* 2012; **27**: 857-864.e1-4 [PMID: 22402229 DOI: 10.1016/j.arth.2012.01.003]
 - 41 **Koyonos L**, Zmistowski B, Della Valle CJ, Parvizi J. Infection control rate of irrigation and débridement for periprosthetic joint infection. *Clin Orthop Relat Res* 2011; **469**: 3043-3048 [PMID: 21553171 DOI: 10.1007/s11999-011-1910-2]
 - 42 **Kuiper JW**, Vos SJ, Saouti R, Vergroesen DA, Graat HC, Debets-Ossenkopp YJ, Peters EJ, Nolte PA. Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention): analysis of risk factors and local antibiotic carriers in 91 patients. *Acta Orthop* 2013; **84**: 380-386 [PMID: 23848215 DOI: 10.3109/17453674.2013.823589]
 - 43 **Fehring TK**, Odum SM, Berend KR, Jiranek WA, Parvizi J, Bozic KJ, Della Valle CJ, Gioe TJ. Failure of irrigation and débridement for early postoperative periprosthetic infection. *Clin Orthop Relat Res* 2013; **471**: 250-257 [PMID: 22552768 DOI: 10.1007/s11999-012-2373-9]
 - 44 **Crockarell JR**, Hanssen AD, Osmon DR, Morrey BF. Treatment of infection with débridement and retention of the components following hip arthroplasty. *J Bone Joint Surg Am* 1998; **80**: 1306-1313 [PMID: 9759815]
 - 45 **Geurts JA**, Janssen DM, Kessels AG, Walenkamp GH. Good results in postoperative and hematogenous deep infections of 89 stable total hip and knee replacements with retention of prosthesis and local antibiotics. *Acta Orthop* 2013; **84**: 509-516 [PMID: 24171687 DOI: 10.3109/17453674.2013.858288]
 - 46 **Engesaeter LB**, Dale H, Schrama JC, Hallan G, Lie SA. Surgical

- procedures in the treatment of 784 infected THAs reported to the Norwegian Arthroplasty Register. *Acta Orthop* 2011; **82**: 530-537 [PMID: 21992085 DOI: 10.3109/17453674.2011.623572]
- 47 **Triantafyllopoulos GK**, Poultsides LA, Zhang W, Sculco PK, Ma Y, Sculco TP. Periprosthetic knee infections treated with irrigation and debridement: outcomes and preoperative predictive factors. *J Arthroplasty* 2015; **30**: 649-657 [PMID: 25466169]
- 48 **Cierny G**, DiPasquale D. Periprosthetic total joint infections: staging, treatment, and outcomes. *Clin Orthop Relat Res* 2002; **(403)**: 23-28 [PMID: 12360003 DOI: 10.1097/00003086-20021000-00005]
- 49 **Burger RR**, Basch T, Hopson CN. Implant salvage in infected total knee arthroplasty. *Clin Orthop Relat Res* 1991; **(273)**: 105-112 [PMID: 1959256 DOI: 10.1097/00003086-199112000-00015]
- 50 **Gardner J**, Gioe TJ, Tatman P. Can this prosthesis be saved?: implant salvage attempts in infected primary TKA. *Clin Orthop Relat Res* 2011; **469**: 970-976 [PMID: 20544317 DOI: 10.1007/s11999-010-1417-2]
- 51 **Chiu FY**, Chen CM. Surgical débridement and parenteral antibiotics in infected revision total knee arthroplasty. *Clin Orthop Relat Res* 2007; **461**: 130-135 [PMID: 17438469 DOI: 10.1097/BLO.0b013e318063e7f3]
- 52 **Bradbury T**, Fehring TK, Taunton M, Hanssen A, Azzam K, Parvizi J, Odum SM. The fate of acute methicillin-resistant *Staphylococcus aureus* periprosthetic knee infections treated by open debridement and retention of components. *J Arthroplasty* 2009; **24**: 101-104 [PMID: 19553077 DOI: 10.1016/j.arth.2009.04.028]
- 53 **Mont MA**, Waldman B, Banerjee C, Pacheco IH, Hungerford DS. Multiple irrigation, debridement, and retention of components in infected total knee arthroplasty. *J Arthroplasty* 1997; **12**: 426-433 [PMID: 9195319]
- 54 **Teeny SM**, Dorr L, Murata G, Conaty P. Treatment of infected total knee arthroplasty. Irrigation and debridement versus two-stage reimplantation. *J Arthroplasty* 1990; **5**: 35-39 [PMID: 2319246 DOI: 10.1016/S0883-5403(06)80007-0]
- 55 **Segawa H**, Tsukayama DT, Kyle RF, Becker DA, Gustilo RB. Infection after total knee arthroplasty. A retrospective study of the treatment of eighty-one infections. *J Bone Joint Surg Am* 1999; **81**: 1434-1445 [PMID: 10535593]
- 56 **Marculescu CE**, Berbari EF, Hanssen AD, Steckelberg JM, Harmsen SW, Mandrekar JN, Osmon DR. Outcome of prosthetic joint infections treated with debridement and retention of components. *Clin Infect Dis* 2006; **42**: 471-478 [PMID: 16421790 DOI: 10.1086/499234]
- 57 **Tattevin P**, Crémieux AC, Pottier P, Hutten D, Carbon C. Prosthetic joint infection: when can prosthesis salvage be considered? *Clin Infect Dis* 1999; **29**: 292-295 [PMID: 10476729 DOI: 10.1086/520202]
- 58 **Li M**, Diep BA, Villaruz AE, Braughton KR, Jiang X, DeLeo FR, Chambers HF, Lu Y, Otto M. Evolution of virulence in epidemic community-associated methicillin-resistant *Staphylococcus aureus*. *Proc Natl Acad Sci USA* 2009; **106**: 5883-5888 [PMID: 19293374 DOI: 10.1073/pnas.0900743106]
- 59 **Martel-Laferrrière V**, Laflamme P, Ghannoum M, Fernandes J, Di Iorio D, Lavergne V. Treatment of prosthetic joint infections: validation of a surgical algorithm and proposal of a simplified alternative. *J Arthroplasty* 2013; **28**: 395-400 [PMID: 23151368 DOI: 10.1016/j.arth.2012.06.034]
- 60 **Peel TN**, Buising KL, Dowsey MM, Aboltins CA, Daffy JR, Stanley PA, Choong PF. Outcome of debridement and retention in prosthetic joint infections by methicillin-resistant staphylococci, with special reference to rifampin and fusidic acid combination therapy. *Antimicrob Agents Chemother* 2013; **57**: 350-355 [PMID: 23114758 DOI: 10.1128/AAC.02061-12]
- 61 **Van Kleunen JP**, Knox D, Garino JP, Lee GC. Irrigation and débridement and prosthesis retention for treating acute periprosthetic infections. *Clin Orthop Relat Res* 2010; **468**: 2024-2028 [PMID: 20224960 DOI: 10.1007/s11999-010-1291-y]
- 62 **Triantafyllopoulos G**, Poultsides LA, Zhang W, Sculco PK, Ma Y, Sculco TP. Multiple Irrigation and Debridements for Periprosthetic Joint Infections: Facing a Necessity or Just Prolonging the Inevitable? *J Arthroplasty* 2016; **31**: 219-224 [PMID: 26216228 DOI: 10.1016/j.arth.2015.06.051]
- 63 **Klouche S**, Lhotellier L, Mamoudy P. Infected total hip arthroplasty treated by an irrigation-debridement/component retention protocol. A prospective study in a 12-case series with minimum 2 years' follow-up. *Orthop Traumatol Surg Res* 2011; **97**: 134-138 [PMID: 21388905 DOI: 10.1016/j.otsr.2011.01.002]

P- Reviewer: Buttaro MA, Fenichel I
S- Editor: Ji FF L- Editor: A E- Editor: Li D



Retrospective Cohort Study

Surgical treatment of Lenke 5 adolescent idiopathic scoliosis: Comparison of anterior vs posterior approach

Mark F Abel, Anuj Singla, Mark A Feger, Lindsay D Sauer, Wendy Novicoff

Mark F Abel, Anuj Singla, Mark A Feger, Lindsay D Sauer, Wendy Novicoff, Department of Orthopedic Surgery, University of Virginia, Charlottesville, VA 22908, United States

Article in press: August 1, 2016
Published online: September 18, 2016

Author contributions: All the authors contributed to this paper.

Institutional review board statement: The study was reviewed and approved for publication by respective Institutional Reviewer Boards.

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at anujrajsingla@gmail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Anuj Singla, MD, Department of Orthopedic Surgery, University of Virginia, P.O. Box 800232, Charlottesville, VA 22908, United States. anujrajsingla@gmail.com
Telephone: +1-434-2430291
Fax: +1-434-2431539

Received: March 22, 2016

Peer-review started: March 23, 2016

First decision: May 16, 2016

Revised: July 19, 2016

Accepted: July 29, 2016

Abstract

AIM

To compare the posterior vs anterior approaches for fusion of Lenke 5 adolescent idiopathic scoliosis curves, matched for curve magnitude and for the distal level of fixation (dLOF) standardized to the third lumbar vertebrae (L3).

METHODS

A prospectively collected multicenter database was used for this retrospective comparative study. Our dependent variables included sagittal and coronal radiographic measurements, number of fused vertebrae, estimated blood loss, length of hospitalization and SRS total and individual domain scores at the two-year follow-up. Subject demographics were similar for all group comparisons. Independent *t*-test was used to compare groups for all analyses at $P < 0.01$.

RESULTS

For all matched cases of Lenke 5 curves, a selective approach was used only 50% of the time in cases undergoing a posterior fusion. When comparing a posterior selective approach to an anterior selective approach, surgeons utilizing a posterior approach fused significantly more levels than surgeons using an anterior approach with no other significant differences in radiographic or SRS outcomes (Ant = 4.8 ± 1.0 levels vs post = 6.1 ± 1.0 levels, $P < 0.0001$). When the dLOF was standardized to L3, the anterior approach provided significantly greater lumbar Cobb percent correction than the posterior approach (Ant = $69.1\% \pm 12.6\%$ vs post = $54.6\% \pm 16.4\%$, $P = 0.004$), with no other significant radiographic or SRS score differences between approaches.

CONCLUSION

Surgeons treating Lenke 5c curves with a posterior instrumentation and fusion *vs* an anterior approach include more motion segments, even with a selective fusion. When controlled for the distal level of fixation, the anterior approach provides greater correction of the thoracolumbar curve.

Key words: Instrumentation; Thoracolumbar curve; Selective fusion

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A multicenter database was analyzed to determine the frequency that surgeons performed a selective fusion of the thoracolumbar (TL)/lumbar curve in adolescent idiopathic scoliosis patients with Lenke 5c curves. We found that surgeons treating Lenke 5c curves will include more motion segments when employing a posterior approach. When controlled for the distal level of fixation, the anterior approach provides greater correction of the TL curve.

Abel MF, Singla A, Feger MA, Sauer LD, Novicoff W. Surgical treatment of Lenke 5 adolescent idiopathic scoliosis: Comparison of anterior *vs* posterior approach. *World J Orthop* 2016; 7(9): 553-560 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/553.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.553>

INTRODUCTION

Lenke 5 curves are the third most common adolescent idiopathic scoliosis (AIS) curve type^[1]. These curves are characterized by a single structural curve in lumbar/thoracolumbar region with non-structural curves (defined as bending to a Cobb angle of less than 25°) in thoracic and low lumbar (lumbosacral) regions of the spine. Common surgical treatment of Lenke 5c curves involves selective fusion (where the proximal level of fixation is distal to the thoracic apex) of the thoracolumbar curve^[1] with the expectation that the non-structural thoracic curve will spontaneously correct^[1-4]. There appears to be good literature support for selective fusion of thoracolumbar curves^[2,4-6]. Ilgenfritz *et al*^[4] studied 21 patients undergoing selective fusion of Lenke 5 curves and identified a spontaneous correction of the uninstrumented thoracic curves of 42% at 1 year. Thirty percent was the correction maintained at five years follow-up^[4]. These authors and others felt that extension of fusion to include thoracic spine provided no significant advantages^[7]. However, there appears to be a state of equipoise in the literature as to whether an anterior or posterior surgical approach is best suited for the selective fusion of Lenke 5 curves.

The anterior approach was initially popularized by Allen Dwyer *et al*^[8] and became increasingly popular

with advancements in anterior instrumentation^[9-11]. The anterior thoracoabdominal approach was reported to be highly efficacious at improving clinical and radiographic measurements of trunk rotation^[10,12]. One important potential advantage of anterior approach was the possibility that surgeons could obtain equal or better correction with shorter fusion constructs and consequently preserve more spinal motion^[12-17].

The posterior approach, however, is more familiar to spine surgeons and the growing popularity of pedicle screws constructs for posterior spinal segmental instrumentation provided a very viable alternate to anterior approach^[18]. Additionally, widespread use of osteotomies^[3] has resulted in better coronal and axial correction^[19-25]. Geck *et al*^[23] compared Lenke 5 AIS correction in 31 patients with posterior pedicle screw instrumented fusion to an equal number of patients undergoing anterior instrumented fusion. The authors^[23] reported significantly better curve correction, less loss of correction over time, and shorter hospital stays with the posterior approach. However, this data represented an AIS cohort that underwent an anterior instrumented fusion from a single institution in comparison to an AIS cohort that underwent a posterior pedicle screw instrumented fusion from a different institution, which makes it difficult to know if differences in blood loss, length of hospitalization, and magnitude of correction are due to differences in surgeon skill or management protocols. Bennett *et al*^[20] reported maintenance of correction with posterior spinal fusion at five years follow-up for a heterogeneous group of Lenke 3c, 5c, and 6c curve types. However, these results cannot be generalized to Lenke 5 curves, as a systematic review by Helenius^[26] suggests that the most appropriate use of the anterior approach is for Lenke 5 curves with a distal level of fixation (dLOF) at third lumbar vertebrae (L3). Evidence suggests that dLOF is significantly correlated with 2-year correction and balance after spinal fusion for Lenke 5 curves^[27], however, previous studies have not matched anterior *vs* posterior cases by dLOF.

To effectively compare these two different approaches in regards to the magnitude of correction, the preservation of motion segments, and patient oriented outcomes for Lenke 5 AIS curves, data is required from multiple surgeons (multi-centered study) with careful regard to match cases according to curve magnitude while standardizing the dLOF at L3. Therefore, our purpose was to compare the posterior *vs* anterior approaches for the instrumentation and fusion of Lenke 5 AIS curve types for cases that were matched by curve magnitude, to compare cases where surgeons used a selective posterior approach (where the proximal level of fixation was distal to the thoracic apex) *vs* anterior cases and to compare selective posterior cases to anterior cases where the dLOF was standardized to the L3. We hypothesized that the anterior approach would result in fewer vertebrae fused and would provide better or comparable correction of radiographic curve parameters when the dLOF was standardized to L3.

MATERIALS AND METHODS

Study design

A prospectively collected multicenter database was used for this cohort study and was queried for all surgically treated Lenke 5c patients. Institutional review board approval for the study was obtained locally from each contributing center and consent was obtained from each patient prior to data collection.

Outcome measures

Radiographic and clinical measurements were recorded pre-operatively and at 2 years after surgery. Our dependent variables were thoracic and lumbar Cobb percent correction, lumbosacral take-off angle (LSTOA) (Figure 1), percent correction, absolute change in thoracolumbar (Th-L) apical translation, change in disc angulation below dLOF, change in proximal junctional kyphosis, change in kyphosis (from T5-T12 and from T10-L2), change in lumbar lordosis (T12 to top of the sacrum), number of fused vertebrae, estimated blood loss, length of hospitalization and SRS total and individual domain scores.

Subjects

Patients with Lenke type 5c deformity were included in the analysis if their curve was corrected by either anterior or posterior spinal fusion. Eighty cases (40 anterior and 40 posterior) were identified and matched according to curve magnitude (Table 1). The surgical approach (anterior vs posterior), as well as the surgical levels fused, were decided by the operating surgeon.

To compare anterior vs posterior surgical approaches, three separate analyses were performed. The first analysis was to compare all matched cases of anterior vs posterior approaches (anterior $n = 40$, posterior $n = 40$). The second analysis compared cases where surgeons used a selective posterior approach (meaning the proximal point of fixation was below the apical vertebra of the thoracic cure) vs selective anterior approaches (anterior selective $n = 39$, posterior selective $n = 20$). The third analysis was to compare selective posterior cases to selective anterior cases where the dLOF was standardized to the L3 (anterior L3 $n = 25$, posterior L3 $n = 14$) (Figure 1).

Statistical analysis

Independent *t*-tests were used to compare anterior and posterior cases for all outcome measures. Our alpha level was conservatively set a priori at 0.01 to control for multiple comparisons. Cohen's *d* effect sizes and associated 95% CIs were calculated for our third analysis (dLOF = L3) to estimate the magnitude and precision of the group differences. Clinical interpretation of effect sizes was performed as > 0.80 was a large effect, 0.50 to 0.79 was a moderate effect, 0.20 to 0.49 was a small effect, and < 0.20 was a trivial effect. Data was analyzed using Statistical Package for Social Sciences (SPSS) Version

20.0 (SPSS, Inc, Chicago, IL).

LSTOA reliability

The angulation of the low lumbar segments (L4 and L5) from the sacrum on the standing film was felt to be an important determinant of coronal plane balance^[28]. Thus the LSTOA^[29], defined from the standing spinal radiograph as the angle between the best-fit line between the spinous processes of L4, L5 and S1 and the vertical, was a radiographic measure developed to assess the influence of instrumentation and fusion on the coronal balance (Figure 2). Four raters of varying experience levels measured pre-operative and 2-year post-operative radiographs for 10 patients on two occasions. Pre-operative and post-operative measurements were separated by at least 24 h and raters were blinded to the first set of measurements during the second measurement occasion. All raters used the same software and all were blinded to one another's measurements until data collection was complete. The reliability of the LSTOA measurement was considered "good" with an intraclass correlation coefficient of 0.829 and Cronbach's alpha value of 0.975.

RESULTS

Demographics and baseline group comparisons

There were no differences in patient demographics for age, height, mass and sex distribution (Ant = 15.1 ± 2.0 years, 163.3 ± 9.6 cm, 56.9 ± 12.1 kg, 8M:32F vs post = 15.4 ± 2.0 years, 159.6 ± 20.2 cm, 59.5 ± 14.1 kg, 6M:34F, $P > 0.01$ for all analyses). There were no significant differences between anterior and posterior cohorts for all cases (anterior $n = 40$, posterior $n = 40$, $P > 0.01$ for all analyses), selective fusions (anterior selective $n = 39$, posterior selective $n = 20$, $P > 0.01$ for all analyses), or selective fusions where dLOF was standardized to L3 (anterior L3 $n = 25$, posterior L3 $n = 14$, $P > 0.01$ for all analyses, Table 1).

All matched cases (anterior $n = 40$, posterior $n = 40$)

The anterior approach resulted in a significantly less number of fused vertebrae (Ant = 4.9 ± 1.1 vs post = 9.0 ± 3.3 , $P < 0.0001$). At 2 years follow-up the radiographic correction, estimated blood loss, length of hospitalization and patient reported SRS scores were noted to be similar for both surgical approaches ($P > 0.01$ for all analyses) (Tables 2 and 3).

Selective posterior fusions vs selective anterior fusions (Ant = 39, post = 20)

There were significantly fewer vertebrae included in the fusion construct when surgeons utilized an anterior approach (Ant = 4.8 ± 1.0 vs post = 6.1 ± 1.0 , $P < 0.0001$). No significant differences were noted between anterior and posterior approaches for measures of radiographic curve parameters, estimated blood loss, length of hospitalization, or SRS scores ($P > 0.01$ for all analyses) (Tables 2 and 3). Representative examples

Table 1 Pre-operative radiographic and self-reported data for anterior and posterior thoraco-lumbar approaches for all cases, selective fusion, and selective fusions where distal level of fixation was the third lumbar vertebra for Lenke 5 curves

	All cases			Selective fusions only			Selective fusions where dLOF = L3		
	Ant (n = 40)	Post (n = 40)	P-value	Ant (n = 39)	Post (n = 20)	P-value	Ant (n = 25)	Post (n = 14)	P-value
Thoracic Cobb	28.7 (7.2)	29.2 (8.0)	0.759	28.3 (6.7)	26.8 (5.7)	0.395	27.6 (5.9)	25.6 (5.5)	0.313
Lumbar Cobb	46.9 (6.7)	47.1 (6.6)	0.880	46.8 (6.7)	48.0 (6.8)	0.0527	47.5 (7.1)	46.6 (6.8)	0.687
LSTOA	15.8 (4.7)	17.0 (5.7)	0.342	15.7 (4.8)	18.3 (6.3)	0.086	15.8 (4.8)	16.3 (4.8)	0.762
Thoracolumbar apical translation (centimeters)	5.0 (1.6)	5.4 (1.5)	0.241	5.0 (1.6)	5.6 (1.7)	0.214	5.2 (1.7)	5.5 (1.3)	0.521
Disc angulation below dLOF (degrees)	0.7 (6.2)	1.9 (5.4)	0.351	0.8 (6.2)	2.3 (5.4)	0.372	2.8 (6.3)	0.4 (4.5)	0.220
Proximal junctional kyphosis (degrees)	4.1 (5.7)	4.7 (4.6)	0.607	4.0 (5.8)	3.2 (2.6)	0.522	4.2 (6.4)	3.2 (2.7)	0.573
Kyphosis from T5-T12 (degrees)	25.7 (10.4)	24.8 (10.0)	0.719	25.7 (10.5)	24.9 (10.2)	0.756	24.4 (10.9)	25.6 (11.1)	0.743
Kyphosis from T10-L2 (degrees)	5.6 (11.3)	3.8 (8.7)	0.437	6.1 (11.0)	7.5 (7.5)	0.622	8.0 (11.7)	5.9 (7.2)	0.547
Lordosis from T12-top of Sacrum (degrees)	60.0 (12.2)	57.4 (10.8)	0.324	60.1 (12.3)	55.7 (11.5)	0.196	57.8 (12.9)	58.9 (8.0)	0.791
SRS (total)	3.9 (0.5)	4.0 (0.3)	0.463	3.9 (0.5)	4.1 (0.3)	0.371	3.9 (0.4)	4.1 (0.3)	0.305
SRS (self)	3.8 (0.7)	3.7 (0.6)	0.367	3.8 (0.7)	3.5 (0.6)	0.335	3.8 (0.5)	3.5 (0.6)	0.282
SRS (pain)	3.7 (0.7)	3.9 (0.6)	0.269	3.6 (0.7)	4.0 (0.4)	0.139	3.6 (0.6)	4.0 (0.4)	0.087
SRS (function)	4.0 (0.6)	4.1 (0.4)	0.469	4.1 (0.6)	4.2 (0.5)	0.392	4.2 (0.4)	4.2 (0.5)	0.691
SRS (activity)	4.5 (0.7)	4.6 (0.5)	0.576	4.5 (0.7)	4.6 (0.6)	0.572	4.5 (0.5)	4.6 (0.6)	0.496

LSTOA: Lumbo-sacral take-off angle; dLOF: Distal level of fixation; T: Thoracic; L: Lumbar; SD: Standard deviation.

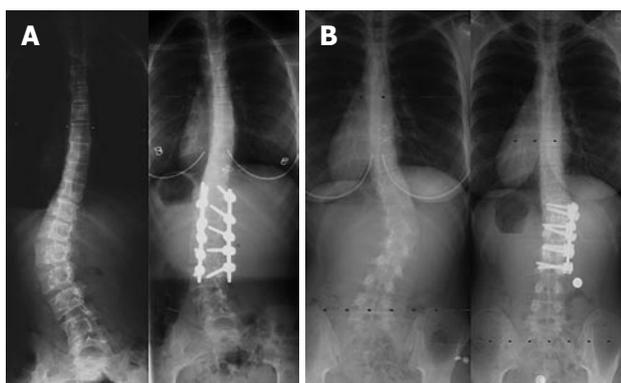


Figure 1 Representative examples for selective posterior (A) and selective anterior (B) spinal fusion.

for selective anterior and posterior approaches are presented in Figure 1.

Selective posterior vs anterior fusions where dLOF = L3 (Ant L3 n = 25, post L3 n = 14)

The anterior approach resulted in a significantly greater lumbar Cobb percent correction (Ant = 69.1% ± 12.6% vs post 54.6% ± 16.4%, *P* = 0.004). No significant differences were noted between anterior and posterior approaches for number of fused vertebrae, radiographic curve parameters, estimated blood loss, length of hospitalization, or SRS scores (*P* > 0.01 for all analyses) (Tables 2 and 3). We identified large effect sizes in favor of the anterior approach for number of fused vertebrae and lumbar Cobb percent correction. We also identified moderate effect sizes in favor of the anterior approach for LSTOA percent correction, absolute change in Th-L

apical translation, and change in disc angulation below the dLOF (L3). All other effect sizes were trivial or small with 95% confidence intervals that were centered around zero, suggesting no meaningful treatment effects for those outcome measures (Figure 3).

DISCUSSION

A primary goal of spinal fusion for idiopathic scoliosis is to maximize correction, while preserving as many motion segments as possible^[4]. Lenke 5 curves are unique in having a thoracolumbar or lumbar curve as the dominant curve in association with a flexible, non-structural thoracic curve, which is expected to spontaneously correct with a selective fusion. We have now provided evidence that for matched Lenke 5 cases and for cases where a selective fusion is performed with similar baseline curve parameters, surgeons performing a posterior approach will include more motion segments in the fusion construct when compared to those performing an anterior approach. In our analyses, including more motion segments did not improve radiographic or patient oriented outcomes^[30]. These findings are particularly important in the context of current evidence highlighting significant reductions in sagittal, coronal, and transverse planes of motion following instrumented spinal fusion^[31]. Furthermore, their results suggest that the more distal the fusion construct goes, the greater reductions in forward flexion post-operatively^[31,32], which underscores the importance of standardizing to the dLOF. Surgeons should continue to rigorously evaluate surgical approaches in clearly defined cohorts to elucidate potential options for maximizing curve correction while maintaining spinal mobility. To our knowledge, this is the first study to

Table 2 Independent *t*-test statistical results for surgical outcomes associated with anterior *vs* posterior thoraco-lumbar approaches for all cases, selective fusions, and selective fusions where distal level of fixation was the third lumbar vertebra for Lenke 5 curves

	All cases			Selective fusions only			Selective fusions where dLOF = L3		
	Ant (n = 40)	Post (n = 40)	P-value	Ant (n = 39)	Post (n = 20)	P-value	Ant (n = 25)	Post (n = 14)	P-value
Thoracic Cobb percent correction	36.7 (23.2)	48.1 (24.3)	0.036	35.9 (22.9)	35 (20.2)	0.890	40.5 (24.6)	37.9 (17.7)	0.732
Lumbar Cobb percent correction	64.5 (14.7)	63.4 (17.0)	0.764	64.7 (14.9)	58.2 (17.1)	0.135	69.1 (12.6)	54.6 (16.4)	0.004 ¹
LSTOA percent correction	46.6 (17.0)	44.9 (21.6)	0.688	46.9 (17.2)	46.2 (21.7)	0.900	48.8 (15.6)	37.7 (19.4)	0.058
Absolute change in thoracolumbar apical translation (centimeters)	3.6 (1.4)	3.2 (1.6)	0.293	3.6 (1.4)	3.5 (1.7)	0.669	3.9 (1.4)	3.2 (1.4)	0.157
Change in disc angulation below dLOF (degrees)	5.2 (9.5)	5.8 (5.0)	0.702	5.1 (9.6)	6.0 (5.7)	0.685	9.0 (7.9)	5.1 (5.7)	0.116
Change in proximal junctional Kyphosis (degrees)	3 (5.2)	4.4 (6.1)	0.253	2.7 (5.0)	2.7 (3.8)	0.989	2.7 (5.7)	3.1 (3.7)	0.806
Change in Kyphosis from T5-T12 (degrees)	-2.4 (9.7)	0.2 (10.3)	0.253	-2.3 (9.8)	-4.4 (8.4)	0.424	-3.5 (10.9)	-5.0 (8.2)	0.652
Change in Kyphosis from T10-L2 (degrees)	24.2 (158.1)	9.6 (8.2)	0.562	25.1 (160.1)	12.4 (8.0)	0.725	39.8 (199.7)	11.2 (8.0)	0.597
Change in Lordosis from T12-Top of sacrum (degrees)	25.0 (148.6)	-1.8 (11.6)	0.261	25.9 (150.5)	-6.0 (10.8)	0.350	39.1 (187.9)	-3.3 (11.0)	0.407
No. of fused vertebrae	4.9 (1.1)	9.0 (3.3)	< 0.001 ¹	4.8 (1.0)	6.1 (1.0)	< 0.001 ¹	5.1 (0.8)	5.8 (1.0)	0.025
Estimated blood loss (mL)	463 (327)	985 (1046)	0.003 ¹	457 (329)	396 (166)	0.441	526 (381)	380 (168)	0.185
Length of hospitalization (d)	5.8 (1.5)	6.0 (1.4)	0.593	5.7 (1.4)	5.8 (1.0)	0.926	6.0 (1.2)	5.6 (1.2)	0.378

¹Denotes significant difference at $P < 0.01$. LSTOA: Lumbo-sacral take-off angle; dLOF: Distal level of fixation; T: Thoracic; L: Lumbar; SD: Standard deviation.

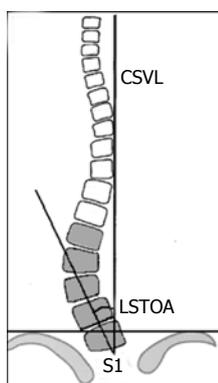


Figure 2 Lumbo-sacral take off angle. LSTOA: Lumbo-sacral take-off angle; CSVL: Central sacral Vertical Line.

compare selective instrumentation and fusion of matched Lenke 5c curves using either a posterior approach *vs* an anterior approach with the dLOF standardized (as recommended)^[26] to the third lumbar level.

In our first analysis, we found that surgeons using a posterior approach to the Lenke 5c deformity included more levels in the instrumentation for comparable curves. This is not a surprising finding given that extension of the posterior exposure and instrumentation is technically easier since the anterior extension requires retraction of the lung, incision of the parietal pleura and control of the segmental vessels proximally or control and mobilization of iliac vessels distally. It should be acknowledged, however, that the relative benefit of complete correction of deformity *vs* the functional loss

from fusing more segments has not been fully elucidated. The tendency to fuse more vertebrae with the posterior approach was also demonstrated in our second analysis of selective posterior *vs* selective anterior cases, yet there was no evidence of superior correction with the posterior approach. Interestingly, half (20 of 40 cases) of our original matched posterior cases were not selective spinal fusions, whereas only 1 of the matched anterior cases had a fusion construct that encompassed the thoracic apex. This finding further illustrates the likelihood of surgeons utilizing a posterior approach to include proximal segments that may or may not be required to improve spinal alignment of the thoracic spine. However, we did identify that surgeons that elected to use a selective posterior fusion fused 5-6 fewer levels than those that utilized a non-selective posterior approach. Finally, when the dLOF was standardized in both groups to L3, the anterior approach provides about a 15% greater correction of the lumbar curve. We also identified moderate to large effect sizes in favor of the anterior approach for outcome measures including number of fused vertebrae, lumbar Cobb percent correction, LSTOA percent correction, absolute change in Th-L apical translation, and change in disc angulation below the dLOF (L3). While the clinical importance of differences of this magnitude is not clearly documented, our results illustrate the potential to maximize post-operative spinal motion with equal or greater radiographic correction with an anterior spinal fusion.

Historically, the anterior approach was considered the preferred approach because of its ability to provide

Table 3 Independent *t*-test statistical results for SRS outcomes associated with anterior *vs* posterior thoraco-lumbar approaches for all cases, selective fusions, and selective fusions where distal level of fixation was the third lumbar vertebra for Lenke 5 curves

	All cases			Selective fusions only			Selective fusions where dLOF = L3		
	Ant (n = 40)	Post (n = 40)	P-value	Ant (n = 39)	Post (n = 20)	P-value	Ant (n = 25)	Post (n = 14)	P-value
Change in SRS (total)	0.15 (0.54)	0.12 (0.53)	0.848	0.19 (0.52)	0.21 (0.31)	0.931	0.14 (0.44)	0.18 (0.32)	0.811
Change in SRS (self)	-0.54 (0.87)	-0.25 (0.93)	0.262	-0.47 (0.83)	-0.14 (0.81)	0.258	-0.40 (0.37)	-0.27 (0.84)	0.632
Change in SRS (pain)	0.49 (0.70)	0.45 (0.83)	0.860	0.55 (0.66)	0.38 (0.56)	0.456	0.48 (0.71)	0.25 (0.53)	0.399
Change in SRS (function)	0.12 (0.66)	-0.09 (0.65)	0.259	0.11 (0.67)	0.05 (0.37)	0.747	-0.03 (0.50)	0.06 (0.42)	0.653
Change in SRS (activity)	0.14 (0.50)	0.06 (0.58)	0.640	0.14 (0.51)	0.17 (0.61)	0.904	0.14 (0.56)	0.21 (0.64)	0.774

T: Thoracic; L: Lumbar; SD: Standard deviation; dLOF: Distal level of fixation.

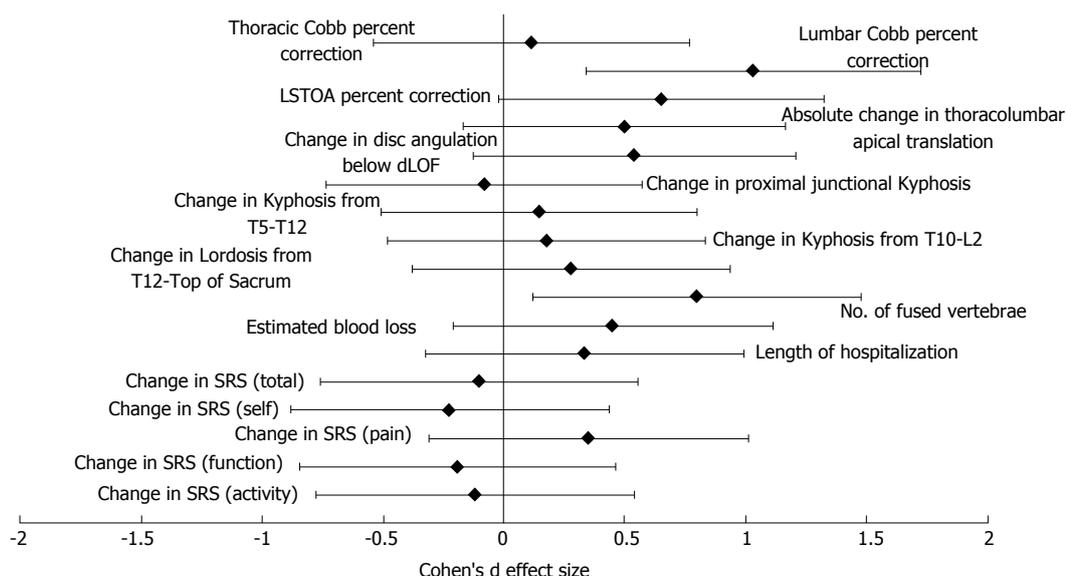


Figure 3 Cohen's d effect sizes and 95%CI for anterior *vs* posterior approach for Lenke 5 adolescent idiopathic scoliosis curves where distal level of fixation is standardized to L3. LSTOA: Lumbo-sacral take-off angle; dLOF: Distal level of fixation; T: Thoracic; L: Lumbar.

excellent coronal curve correction with significant spine derotation and shorter fusion constructs^[5-9]. Tao *et al*^[14] reported superiority of anterior solid rod-screw instrumentation with shorter fusion segments, better sagittal alignment and quality of life measures (SRS scores) than posterior pedicle screw instrumentation. However, trunk scarring, spine pseudoarthrosis, negative impacts on pulmonary function and reduction of lumbar lordosis were reported to be major disadvantages of the anterior approach^[24]. More recent studies with newer techniques and implant designs have reported no significant post-operative kyphosis^[12] or pulmonary function changes^[33] with the anterior thoracoabdominal approach. Our results are consistent with the recent studies in that there were no differences in patient oriented outcomes as reported on the SRS questionnaires or in EBL or length of hospitalization between anterior or posterior approaches for any of our three analyses.

This study has several limitations. Matching was based on radiographic measures but surgeons may have chosen the surgical approach based on the clinical appearance, extending the fusion to include the thoracic vertebra in cases with a more pronounced right scapular prominence. The sagittal plane alignment of either

the lumbar and thoracic curves can also influence the decision on the surgical approach. For instance, increased lumbar kyphosis, excessive thoracic kyphosis or thoracic hyper-lordosis, may prompt the surgeon to use a posterior approach for instrumentation to affect sagittal plane correction and this was not analyzed. An argument could also be made that the magnitude of difference between these two approaches is not meaningful to the patient, as we did not identify significant differences in our SRS outcomes or length of hospitalization between approaches. The relative benefits of complete correction of deformity *vs* the functional loss from fusing more segments has not been objectively studied. However, until we have more objective data on the functional implications of longer fusions or the rate of adjacent level degeneration, we cannot strongly advise an anterior TL approach for the Lenke 5C curve. Given the above considerations, our results do suggest that an anterior approach may be advantageous for severe or rigid deformity where the desired dLOF is the third lumbar level (Figure 1), as it can provide better correction for same levels of fusion with no deleterious effects on patient reported outcomes.

In conclusion, surgeons treating Lenke 5c curves

will include more motion segments when employing a posterior approach; when controlled for the dLOF, the anterior approach provides greater correction of the TL curve.

COMMENTS

Background

Lenke 5 scoliosis can be surgically corrected by either anterior or posterior approach. The purpose of this study purpose was to compare the posterior vs anterior approaches for fusion of Lenke 5 adolescent idiopathic scoliosis curves.

Research frontiers

Posterior approach is more popular nowadays because of its ease and universal application. Anterior approach is generating interest again because of its ability to provide excellent coronal curve correction and significant spine derotation with relatively shorter fusion constructs. The current research is also focused on saving fusion levels, which may prove to be an important factor in the long term.

Innovations and breakthroughs

To our knowledge, this is the first study to compare selective instrumentation and fusion of matched Lenke 5c curves with the distal level of fixation (dLOF) standardized to the third lumbar level, in addition to overall surgical outcome of anterior vs posterior approaches.

Applications

This study suggests a tendency to fuse more levels with posterior approach for treating Lenke 5c curves and that the anterior approach provides greater correction for similar distal level of fusion. These findings may provide important guidelines with regards to surgical approach if surgeon prefers shorter fusion levels for deformity correction.

Terminology

Distal level of fixation - dLOF.

Peer-review

Interesting paper that compares two different approaches for surgical correction of Lenke 5c scoliosis by selective fusion.

REFERENCES

- 1 **Lenke LG**, Betz RR, Clements D, Merola A, Hafer T, Lowe T, Newton P, Bridwell KH, Blanke K. Curve prevalence of a new classification of operative adolescent idiopathic scoliosis: does classification correlate with treatment? *Spine (Phila Pa 1976)* 2002; **27**: 604-611 [PMID: 11884908 DOI: 10.1097/00007632-200203150-00008]
- 2 **Senkoylu A**, Luk KD, Wong YW, Cheung KM. Prognosis of spontaneous thoracic curve correction after the selective anterior fusion of thoracolumbar/lumbar (Lenke 5C) curves in idiopathic scoliosis. *Spine J* 2014; **14**: 1117-1124 [PMID: 24120146 DOI: 10.1016/j.spinee.2013.07.467]
- 3 **Huitema GC**, Jansen RC, van Ooij A, Punt IM, van Rhijn LW. Predictability of spontaneous thoracic curve correction after anterior thoracolumbar correction and fusion in adolescent idiopathic scoliosis. A retrospective study on a consecutive series of 29 patients with a minimum follow-up of 2 years. *Spine J* 2015; **15**: 966-970 [PMID: 23958296 DOI: 10.1016/j.spinee.2013.06.013]
- 4 **Ilggenfritz RM**, Yaszay B, Bastrom TP, Newton PO. Lenke 1C and 5C spinal deformities fused selectively: 5-year outcomes of the uninstrumented compensatory curves. *Spine (Phila Pa 1976)* 2013; **38**: 650-658 [PMID: 23089928 DOI: 10.1097/BRS.0b013e3182793092]
- 5 **Huitema GC**, Jansen RC, Dompeling E, Willems P, Punt I, van Rhijn LW. Pulmonary function after less invasive anterior instrumentation and fusion for idiopathic thoracic scoliosis. *Scoliosis* 2013; **8**: 14 [PMID: 23965278 DOI: 10.1186/1748-7161-8-14]
- 6 **Min K**, Hahn F, Ziebarth K. Short anterior correction of the thoracolumbar/lumbar curve in King I idiopathic scoliosis: the behaviour of the instrumented and non-instrumented curves and the trunk balance. *Eur Spine J* 2007; **16**: 65-72 [PMID: 16544158 DOI: 10.1007/s00586-006-0075-2]
- 7 **Lark RK**, Yaszay B, Bastrom TP, Newton PO. Adding thoracic fusion levels in Lenke 5 curves: risks and benefits. *Spine (Phila Pa 1976)* 2013; **38**: 195-200 [PMID: 22691919 DOI: 10.1097/BRS.0b013e3182634c85]
- 8 **Dwyer AF**, Newton NC, Sherwood AA. An anterior approach to scoliosis. A preliminary report. *Clin Orthop Relat Res* 1969; **62**: 192-202 [PMID: 5774835]
- 9 **Halm H**, Richter A, Thomsen B, Köszevgy M, Ahrens M, Quante M. [Anterior scoliosis surgery. State of the art and a comparison with posterior techniques]. *Orthopade* 2009; **38**: 131-134, 136-140, 142-145 [PMID: 19198802 DOI: 10.1007/s00132-008-1365-7]
- 10 **Kaneda K**, Shono Y, Satoh S, Abumi K. New anterior instrumentation for the management of thoracolumbar and lumbar scoliosis. Application of the Kaneda two-rod system. *Spine (Phila Pa 1976)* 1996; **21**: 1250-1261; discussion 1261-1262 [PMID: 8727201 DOI: 10.1097/00007632-199605150-00021]
- 11 **Hall JE**. Dwyer Instrumentation in anterior fusion of the spine. *J Bone Joint Surg Am* 1981; **63**: 1188-1190 [PMID: 7276060]
- 12 **Verma K**, Auerbach JD, Kean KE, Chamas F, Vorsanger M, Lonner BS. Anterior spinal fusion for thoracolumbar scoliosis: comprehensive assessment of radiographic, clinical, and pulmonary outcomes on 2-years follow-up. *J Pediatr Orthop* 2010; **30**: 664-669 [PMID: 20864850 DOI: 10.1097/BPO.0b013e3181ec931b]
- 13 **Wang T**, Zeng B, Xu J, Chen H, Zhang T, Zhou W, Kong W, Fu Y. Radiographic evaluation of selective anterior thoracolumbar or lumbar fusion for adolescent idiopathic scoliosis. *Eur Spine J* 2008; **17**: 1012-1018 [PMID: 17912556 DOI: 10.1007/s00586-007-0510-z]
- 14 **Tao F**, Wang Z, Li M, Pan F, Shi Z, Zhang Y, Wu Y, Xie Y. A comparison of anterior and posterior instrumentation for restoring and retaining sagittal balance in patients with idiopathic adolescent scoliosis. *J Spinal Disord Tech* 2012; **25**: 303-308 [PMID: 21666508 DOI: 10.1097/BSD.0b013e3182204c3e]
- 15 **Lu WC**, Zhang JG, Qiu GX, Sadik I, Wang YP, Yu B, Zhao H, Zhao Y, Weng XS. [Selective anterior thoracolumbar or lumbar fusion for adolescent idiopathic scoliosis]. *Zhonghua Waike Zazhi* 2009; **47**: 758-761 [PMID: 19615212]
- 16 **Liu Y**, Li M, Zhu XD, Zhou XH, Chen HJ, Wang XW, Shi P, Yuan W. Retrospective analysis of anterior correction and fusion for adolescent idiopathic thoracolumbar/lumbar scoliosis: the relationship between preserving mobile segments and trunk balance. *Int Orthop* 2009; **33**: 191-196 [PMID: 18188567 DOI: 10.1007/s00264-007-0489-4]
- 17 **Lowe TG**, Betz R, Lenke L, Clements D, Harms J, Newton P, Hafer T, Merola A, Wenger D. Anterior single-rod instrumentation of the thoracic and lumbar spine: saving levels. *Spine (Phila Pa 1976)* 2003; **28**: S208-S216 [PMID: 14560194 DOI: 10.1097/01.BRS.0000092483.10776.2A]
- 18 **Potter BK**, Kuklo TR, Lenke LG. Radiographic outcomes of anterior spinal fusion versus posterior spinal fusion with thoracic pedicle screws for treatment of Lenke Type I adolescent idiopathic scoliosis curves. *Spine (Phila Pa 1976)* 2005; **30**: 1859-1866 [PMID: 16103856 DOI: 10.1097/01.brs.0000174118.72916.96]
- 19 **Gu SX**, Li M, Zhu XD, Wang CF, Wu DJ, Zhao YC. Posterior pedicle screws combined with shortening and release techniques for lumbar and thoracolumbar adolescent idiopathic scoliosis. *Orthop Surg* 2009; **1**: 6-11 [PMID: 22009774 DOI: 10.1111/j.2757-7861.2008.00002.x]
- 20 **Bennett JT**, Hoashi JS, Ames RJ, Kimball JS, Pahys JM, Samdani AF. The posterior pedicle screw construct: 5-year results for thoracolumbar and lumbar curves. *J Neurosurg Spine* 2013; **19**: 658-663 [PMID: 24074506 DOI: 10.3171/2013.8.SPINE12816]
- 21 **Huang Z**, Wang Q, Yang J, Yang J, Li F. Vertebral Derotation by

- Vertebral Column Manipulator Improves Postoperative Radiographs Outcomes of Lenke 5C Patients for Follow-up of Minimum 2 Years. *Clin Spine Surg* 2016; **29**: E157-E161 [PMID: 27007792 DOI: 10.1097/BSD.000000000000123]
- 22 **Hwang SW**, Dubaz OM, Ames R, Rothkrug A, Kimball JS, Samdani AF. The impact of direct vertebral body derotation on the lumbar prominence in Lenke Type 5C curves. *J Neurosurg Spine* 2012; **17**: 308-313 [PMID: 22860878 DOI: 10.3171/2012.7.SPINE12273]
- 23 **Geck MJ**, Rinella A, Hawthorne D, Macagno A, Koester L, Sides B, Bridwell K, Lenke L, Shufflebarger H. Comparison of surgical treatment in Lenke 5C adolescent idiopathic scoliosis: anterior dual rod versus posterior pedicle fixation surgery: a comparison of two practices. *Spine (Phila Pa 1976)* 2009; **34**: 1942-1951 [PMID: 19680102 DOI: 10.1097/BRS.0b013e3181a3c777]
- 24 **Shufflebarger HL**, Geck MJ, Clark CE. The posterior approach for lumbar and thoracolumbar adolescent idiopathic scoliosis: posterior shortening and pedicle screws. *Spine (Phila Pa 1976)* 2004; **29**: 269-276; discussion 276 [PMID: 14752348 DOI: 10.1097/01.BRS.0000109881.63411.48]
- 25 **Okada E**, Watanabe K, Pang L, Ogura Y, Takahashi Y, Hosogane N, Toyama Y, Matsumoto M. Posterior correction and fusion surgery using pedicle-screw constructs for Lenke type 5C adolescent idiopathic scoliosis: a preliminary report. *Spine (Phila Pa 1976)* 2015; **40**: 25-30 [PMID: 25526588 DOI: 10.1097/BRS.0000000000000652]
- 26 **Helenius I**. Anterior surgery for adolescent idiopathic scoliosis. *J Child Orthop* 2013; **7**: 63-68 [PMID: 24432061 DOI: 10.1007/s11832-012-0467-2]
- 27 **Wang Y**, Bünger CE, Zhang Y, Wu C, Li H, Dahl B, Hansen ES. Lowest instrumented vertebra selection for Lenke 5C scoliosis: a minimum 2-year radiographical follow-up. *Spine (Phila Pa 1976)* 2013; **38**: E894-E900 [PMID: 23574819 DOI: 10.1097/BRS.0b013e31829537be]
- 28 **Mehta SS**, Modi HN, Srinivasalu S, Chen T, Suh SW, Yang JH, Song HR. Interobserver and intraobserver reliability of Cobb angle measurement: endplate versus pedicle as bony landmarks for measurement: a statistical analysis. *J Pediatr Orthop* 2009; **29**: 749-754 [PMID: 20104157 DOI: 10.1097/BPO.0b013e3181b72550]
- 29 **Abel MF**, Herndon SK, Sauer LD, Novicoff WM, Smith JS, Shaffrey CI. Selective versus nonselective fusion for idiopathic scoliosis: does lumbosacral takeoff angle change? *Spine (Phila Pa 1976)* 2011; **36**: 1103-1112 [PMID: 21245788 DOI: 10.1097/BRS.0b013e3181f60b5b]
- 30 **Singla A**, Bennett JT, Sponseller PD, Pahys JM, Marks MC, Lonner BS, Newton PO, Miyanji F, Betz RR, Cahill PJ, Samdani AF. Results of selective thoracic versus nonselective fusion in Lenke type 3 curves. *Spine (Phila Pa 1976)* 2014; **39**: 2034-2041 [PMID: 25271497 DOI: 10.1097/BRS.0000000000000623]
- 31 **Udoekwere UI**, Krzak JJ, Graf A, Hassani S, Tarima S, Riordan M, Sturm PF, Hammerberg KW, Gupta P, Anissipour AK, Harris GF. Effect of Lowest Instrumented Vertebra on Trunk Mobility in Patients With Adolescent Idiopathic Scoliosis Undergoing a Posterior Spinal Fusion. *Spine Deformity* 2014; **2**: 291-300 [DOI: 10.1016/j.jspd.2014.04.006]
- 32 **Sun X**, Qiu Y, Liu Z, Ma WW, Wang B, Zhu ZZ, Yu Y, Qian BP, Zhu F. Interbody cage support improves reconstruction of sagittal balance after anterior selective fusion in Lenke type 5 idiopathic scoliosis patients. *Orthop Surg* 2009; **1**: 285-292 [PMID: 22009877 DOI: 10.1111/j.1757-7861.2009.00051.x]
- 33 **Kim YJ**, Lenke LG, Bridwell KH, Cheh G, Sides B, Whorton J. Prospective pulmonary function comparison of anterior spinal fusion in adolescent idiopathic scoliosis: thoracotomy versus thoracoabdominal approach. *Spine (Phila Pa 1976)* 2008; **33**: 1055-1060 [PMID: 18449037 DOI: 10.1097/BRS.0b013e318116fc3a5]

P- Reviewer: Elgafy H, Korovessis P S- Editor: Qiu S
L- Editor: A E- Editor: Li D



Observational Study

Attitudes and diagnostic practice in low back pain: A qualitative study amongst Greek and British physiotherapists

Evdokia Billis, Christopher J McCarthy, John Gliatis, Charalampos Matzaroglou, Jacqueline A Oldham

Evdokia Billis, Charalampos Matzaroglou, Department of Physical Therapy, Technological Educational Institute of Western Greece, 25100 Aigion, Greece

Christopher J McCarthy, Imperial College Healthcare NHS Trust, St Mary's Hospital, Paddington, London W2 1NY, United Kingdom

John Gliatis, Department of Orthopaedic, University Hospital of Patras, 25100 Patras, Greece

Jacqueline A Oldham, University of Manchester, Manchester: Integrating Medicine and Innovative Technology, Manchester M13 9NQ, United Kingdom

Author contributions: Billis E designed the research, conducted the data collection and analysis and wrote the manuscript; McCarthy CJ contributed to the conception of the design and facilitated data collection amongst British physiotherapists; Gliatis J contributed to the data interpretation and analysis of this design; Matzaroglou C assisted in data collection and proof reading of this article; Oldham JA was responsible for making critical revisions to the conceptual content of the manuscript and conducted the final approval of the manuscript.

Supported by The MACP's Elsevier Science and Doctoral Awards for Research in Manipulative Physiotherapy.

Institutional review board statement: The study was reviewed and approved by the Ethical Committees of Technological Educational Institute (TEI) of Lamia, Greece and University of Manchester, United Kingdom.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: There are no conflicts of interest to report.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external

reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Evdokia Billis, Assistant Professor in Physiotherapy, Department of Physical Therapy, Technological Educational Institute of Western Greece, Psaron 6, 25100 Aigion, Greece. ebillis@teiwest.gr
 Telephone: +30-26-91061150
 Fax: +30-26-91061250

Received: February 22, 2016
 Peer-review started: February 23, 2016
 First decision: March 25, 2016
 Revised: April 21, 2016
 Accepted: June 27, 2016
 Article in press: June 29, 2016
 Published online: September 18, 2016

Abstract

AIM

To explore current diagnostic practice and attitudes of Greek and United Kingdom physiotherapists (PTs) on assessing low back pain (LBP) patients.

METHODS

Three focus groups were undertaken, followed by a structured questionnaire-type survey comprising 23 health professionals and a random stratified sample of 150 PTs, respectively. Twenty-nine themes relating to LBP diagnostic practice emerged. These were then given to 30 British PTs assessing their level of

agreement with their Greek counterparts. Analysis was performed by percentage agreements and χ^2 tests.

RESULTS

The survey was divided into three subsections; PTs' attitudes on LBP assessment, patients' attitudes and diagnostic/healthcare issues, each constituting 14, 7 and 8 statements, respectively. Over half of the statements fell within the 30%-80% agreement between Greece and United Kingdom whereas, 5 statements reported low (< 10%) and 8 statements demonstrated high (> 90%) PT percentage agreement. Similarities across British and Greek PTs were detected in history taking methods and in the way PTs feel patients perceive physiotherapy practice whereas, re-assessment was undertaken less frequently in Greece. Diagnosis according to 91% of the Greek PTs is considered a "privilege" which is exclusive for doctors in Greece (only 17% British PTs agreed) and is accompanied with a great overuse of medical investigations. Forty percent of Greek PTs (compared to 0% of British) consider themselves as "executors", being unable to interfere with treatment plan, possibly implying lack of autonomy.

CONCLUSION

Although similarities on history taking methods and on patients' attitudes were detected across both groups, gross differences were found in re-assessment procedures and diagnostic issues between Greek and British physiotherapists, highlighting differences in service delivery and professional autonomy.

Key words: Diagnostic practice; Low back pain; United Kingdom; Greek; Physiotherapists

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This small-scale observational study explored commonalities and differences in low back pain (LBP) perspectives and diagnostic practice between Greek and British physiotherapists (PTs). There was agreement on clinical examination features for targeting treatment; indicating that LBP is a clinical entity whose clinical "expressions" amongst PTs and patients are common across different cultural groups. The differences detected particularly referred to diagnostic issues (*i.e.*, overuse of medical investigations/radiography, *etc.*), reflecting differences in medical and physiotherapy services delivery. Such comparisons contribute to the understanding of the course and/or management of LBP across the two countries.

Billis E, McCarthy CJ, Gliatis J, Matzaroglou C, Oldham JA. Attitudes and diagnostic practice in low back pain: A qualitative study amongst Greek and British physiotherapists. *World J Orthop* 2016; 7(9): 561-569 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/561.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.561>

INTRODUCTION

Low back pain (LBP) is a highly prevalent problem both within the Greek and British cultural settings, notorious for causing debilitating, economic, psychosocial, and behavioural problems. Within Greece, it is considered ninth in the list of the most common reasons requiring hospital admission^[1], first in the list of orthopaedic conditions being encountered in an emergency department^[2]. LBP also seems to be the most common musculoskeletal problem amongst the Greek general^[3-5] and occupational populations^[6-10]; with point and annual prevalence rates ranging between 11%-31.7% amongst adults^[3,4]. High prevalence rates are also seen across the general population within Great Britain; point and one-month prevalence rates are estimated between 19%-21% whereas, annual and lifetime prevalence rates range between 29%-43% and 58%-64%, respectively^[11-15]. Thus, it is evident that in both countries, LBP is a widespread public health problem, often leading to chronicity as well as disability^[4,5,11,16,17].

In terms of the healthcare seeking patterns, one of the first-line health professionals involved in the management of LBP within Greece^[7,8], Britain^[11,18], as well as internationally^[19,20] are physiotherapists (PTs)^[2,8,11,13,21,22]. Subsequently, research has turned towards exploring a number of issues dealing with the assessment and treatment aspects of healthcare practice and practitioners, to improve patient care and outcomes.

Clinicians perform a thorough assessment and develop their clinical hypothesis, in order to formulate an objective clinical diagnosis for their patient and determine their intervention plan^[23]. However, it has been suggested that their attitudes and beliefs towards assessment issues influence their clinical diagnosis and subsequent treatment decisions. Fullen *et al.*^[24-26] in a series of studies and systematic reviews explored the factors that impact on doctors' management of LBP patients; they found that, amongst other things, clinicians' attitudes and beliefs influence their management approach. Perreault and Dionne have found discrepancies between PTs' and patients' perceptions of LBP experience, which have been partly attributed to the PTs' attitudes and beliefs regarding pain-related issues^[27]. Similar findings were reported in other studies too, relating attitudes and beliefs of a range of health professionals (including PT), to their assessment and treatment strategies for LBP patients^[28,29]. Therefore, it appears that, health professionals' attitudes and beliefs are associated to their diagnostic and management practice.

It has been suggested that cultural differences amongst healthcare professionals tend to "shape" particular attitudes, beliefs and perspectives, which subsequently affect the patients' overall management approach. For example, whilst in some European countries such as Great Britain^[30] and the Netherlands^[31], radiography (X-ray) utilisation was found to be in accordance with current guideline practice, diagnostic

imaging has been reported to be overprescribed across a number of other countries such as Italy^[32], Belgium^[33], Norway^[34], Canada^[35], Brazil^[36] and the United States^[37], thus, highlighting cross-cultural health professionals' differences in LBP diagnostic practice regarding X-ray utilisation.

Skelton *et al.*^[38] investigated the perceptions of British general practitioners (GPs) regarding their LBP patients, and found that the GPs perception of their patient's psychological constitution, occupation and social class were found to be important factors in determining their clinical approach and behaviour. In another British survey, the attitudes and beliefs of GPs and PTs regarding LBP were explored^[30]. A considerable proportion of the health professionals adopted a biomedical (rather than biopsychosocial) approach in their diagnostic practice, thus, taking into account only the pathologic and physical processes of the LBP problem but not the social or psychological influences. Similar conclusions were yielded by a French study exploring the fear-avoidance beliefs of a large GP sample^[39]. Fear-avoidance beliefs, which are believed to play a role in chronic disability, are related to pain-related interpretations that activity will cause injury and eventually exacerbate pain. In this study^[39], high levels of fear-avoidance beliefs were reported amongst French GPs, which impacted in the recommendations given to patients regarding physical activity and work. Thus, based on the above, there is evidence that health professionals' diagnostic behaviours and management approaches are not exclusively attributed to medical factors but are also influenced by cultural factors and individual perspectives^[40].

There is limited research investigating PTs' attitudes and beliefs on LBP assessment and "diagnostic" issues within a number of cultural settings, including the Greek and British ones. Thus, issues linking PTs' perspectives, attitudes, and behaviours to diagnostic practice across the two settings merited further investigation. The aim of this study was to compare current diagnostic practice and attitudes of Greek and British physiotherapists when assessing and treating LBP patients.

MATERIALS AND METHODS

The study was divided into three parts. In the first component, as part of an study described elsewhere^[41], a list of issues relating to current diagnostic practice and attitudes of clinicians on LBP assessment within Greece were developed following three focus groups involving 23 health professionals (18 PTs and 5 doctors). In the second component, the issues raised by the PTs (from the focus groups) were given to a wider PT sample in a questionnaire format (Delphi-type survey), to assess their level of agreement with each statement. In the last part, these items were also given to a British PT sample, to assess their level of agreement. Ethical approval was obtained from the Ethical Committees of Technological Educational Institute of Lamia, Greece and University of Manchester, United Kingdom.

Sample

Greek participants, consisted of Greek PTs, randomly selected from data obtained by the Panhellenic Physiotherapy Association (PPA), the official body representing chartered PTs in Greece. Out of the approximately 1500 registered members at the time of the study, 10% (150 PTs) was invited to participate. The sample was further stratified according to geographical location and work status, to obtain greater representation. For geographical location, Greece was divided into 7 areas; 2 urban, representing the 2 biggest cities (Athens and Thessaloniki), and 5 rural ones (North, South, Central, East and West of Greece). For work status, PTs were stratified according to private or public sector, as PPA data revealed a disproportionately high percentage of PTs working in the private compared to the public sector.

The British sample was a convenience sample consisting of 30 Chartered PTs working in the private or public sector, who were at the time involved in another study^[42].

Procedure

Overall, 29 statements were collected from the PTs' focus groups, divided into three sections; PTs' attitudes, patients' attitudes and health/diagnostic issues. Generating data by other qualitative means for developing a structured questionnaire is an acceptable, recommended and commonly used method^[43-45]. The items were collated into a single list and transformed into a structured questionnaire with 5-point Likert scale answers ("Strongly Agree", "Agree", "Neither Agree or Disagree", "Disagree", "Strongly Disagree"), where PTs were requested to vote on their agreement. For the Greek questionnaire, all questions/statements were reviewed by 2 native (Greek) researchers for clarity and objectivity. Overall, 150 questionnaires were posted to all PTs including the informed consent and a demographic information sheet. For the British questionnaire, each statement was transcribed into the English language by the principal investigator and two native (English) speakers reviewed the questionnaire for grammar, syntax, clarity and comprehensibility. Questionnaires were administered electronically, as electronic surveying is an acceptable and popular method of collecting data across the musculoskeletal field^[46-48]. A consent form and a demographic information sheet were also provided.

Additional space was also allocated for further comments in both questionnaires; however, no additional comments were made. Three to five weeks were given for the PTs' replies prior to sending a reminder.

Data analysis

The questionnaires were analysed utilizing percentage agreements for each scored item, utilising SPSS (Version 11.5). Percentage agreement was calculated by utilising the two agreement options ("Strongly Agree" and "Agree") from the Likert scale. The χ^2 test was used to determine associations between Greek and British PTs' as well as differences between survey's responses.

Table 1 Physiotherapists' profile

Characteristics	Greek PTs (<i>n</i> = 125) [% (<i>n</i>)]	British PTs (<i>n</i> = 29) [% (<i>n</i>)]	<i>P</i> value (χ^2 test)
Sex			
Male	57.6 (72)	24.1 (7)	0.053
Female	39.2 (49)	51.7 (15)	
Missing data/not reported	3.2 (4)	24.1 (7)	
LBP clinical experience (yr)			
< 1	3.2 (4)	3.4 (1)	0.002 ¹
1-5	28 (35)	3.4 (1)	
6-10	28 (35)	24.1 (7)	
> 11	40.8 (51)	65.2 (19)	
Type of work			
NHS based	35.2 (44)	75.8 (22)	0.671
Private practitioner	49.6 (62)	6.8 (2)	
Community work (private)	10.4 (13)	3.4 (1)	
Other (educational, etc.)	4.8 (6)	6.8 (2)	

¹ χ^2 test is statistically significant at the 0.05 level. PTs: Physiotherapists; LBP: Low back pain; NHS: National Health Service.

RESULTS

Overall, 125 Greek and 29 British questionnaires were returned (response rates of 83.3% and 96.6%, respectively). For the Greek PTs, all geographical areas were represented entailing the following number of PTs: For Athens 55 (44%), Thessaloniki 15 (12%), South 10 (8%), North 8 (6.4%), Central 15 (12%), East 11 (8.8%) and West of Greece 10 (8%). Over half of the sample (60%) was working in the private sector compared to 35.2% who were based within a NHS establishment. Over half of the sample (57.6%) was males, and the majority had more than 6 years of clinical experience with LBP patients (68.8%). Most of the convenience British sample had more than 6 years of LBP clinical experience (89.3%) and were NHS-based PTs (75.8%). χ^2 tests across the two PT groups on sex and type of work yielded non-statistically significant results ($P > 0.05$), indicating similarities (on these variables) across the samples between the two groups, whereas statistically significant differences ($P = 0.002$) were yielded for clinical experience. The sample's profile is illustrated in Table 1.

The questionnaire consisted of 29 statements which were divided into three subsections (PTs' attitudes, patients' attitudes and diagnostic/healthcare issues), each constituting 14, 7 and 8 statements, respectively. Over half of the statements fell within the 30% to 80% range. Five statements (all from the British PTs) reported low (below 10%) percentage agreement (small history taking, not taking into account psychosocial factors, lack of emphasis in undergraduate assessment, overuse of medical investigations, PTs are "executers", etc.).

Whereas, eight statements (5 from Greek and 3 from British PTs) demonstrated agreement for over 90% of the PTs; history guides assessment and paying attention to the medical diagnosis (British PTs), detailed history taking (both groups), alteration of examination for acute/chronic patients, diagnosis as a medical privilege, diagnosing as part of physiotherapy practice and lack of emphasis in undergraduate assessment.

Fifteen out of the 29 statements yielded statistically significant differences across the two PT groups. These, were 7 statements from PTs Attitudes subsection (letting patient talk during assessment, history guides assessment, paying attention to the medical diagnosis and referral card and sequence of re-assessment), two statements from patients' attitudes subsection (sick leave in relation to working on public or private sector and understand patient's psychosocial problems following several treatment sessions) and 6 statements from Diagnostic Issues subsection (diagnosis as a medical privilege, diagnosing as part of physiotherapy practice, lack of emphasis in undergraduate assessment, PTs are executers, overuse of medical investigations and more emphasis on laboratory investigations). Table 2 illustrates percentage agreements and statistical results for each statement amongst the cultural groups.

In summary the data shows that both countries PTs agreed on the need for a thorough clinical examination, including assessment for serious pathology. There was disagreement from the United Kingdom physiotherapists regarding the frequency of reassessment, the right to diagnose, the over-investigation of LBP and the need for more undergraduate training in low back pain.

DISCUSSION

This study explored diagnostic practice and attitudes between Greek and British PTs in assessing LBP patients, utilising a questionnaire-based comparison, the content of which was developed by Greek PTs' focus groups^[41].

PTs' attitudes towards assessment

A large number of similarities amongst the two cultural groups were reported in the PTs' assessment section. Both PT groups agreed on taking notes with a detailed history of the patient during the first visit, including the examination of non-musculoskeletal causes (red flags) and including reassessment following every PT session. There was also low agreement that their examina-

Table 2 Percentage agreements amongst the Greek and British physiotherapists

Opinions/statements	Greek PTs (%)	British PTs (%)	P value (χ^2 test)
PTs' attitudes towards assessment			
I take a small history the first time (within the first assessment), so as to proceed to the therapy straightaway	15.8	0	0.325
I take a very detailed history the first time trying to locate the patient's problem	91	96.6	0.998
Throughout my formal assessment, I don't take into account the patient's psychosocial status because I believe that the biomedical dimension is the patient's main problem	17.1	3.6	0.476
I let the patient talk (without interruptions) about his problem. This helps the impression I gain about his psychosocial status	72.2	44.8	0.039 ¹
I use notes/assessment forms	61.8	79	0.084
The patient's symptoms are what guides history taking and clinical assessment <i>i.e.</i> , if symptoms look like a nerve root problem, then the clinical examination will focus more on neurological/neurodynamic examination	53.7	96.6	0.001 ²
Once doctors have excluded any red flags/serious pathology from their patient, they then are not interested in further distinguishing, diagnosing or sub-classifying the patient's back pain	77.3	58.6	0.562
I believe that physiotherapy assessment should include the assessment of non-musculoskeletal nature of back pain (<i>i.e.</i> , red flag type questions and clinical tests)	77	100	0.128
I pay attention to the doctor's medical diagnosis	42.6	96.6	< 0.001 ²
I pay attention to the doctor's referral card	13.8	62.1	< 0.001 ²
I alter my examination based on whether my patient is acute or chronic	97.3	69	< 0.001 ²
I reassess each patient (looking for exacerbation or improvement) before and/or following every treatment procedure (thus, within each treatment session)	44.9	89.7	0.004 ¹
I reassess each patient (looking for exacerbation or improvement) following every treatment session only	70	86.2	0.745
I reassess each patient (looking for exacerbation or improvement) following 4-5 treatment sessions only	72	41.4	0.011 ¹
Patients' attitudes towards assessment			
You start getting a feel of the patient's psychosocial problems, after you start develop a relationship with the patient (that is, following several treatment sessions)	58.1	13.8	0.002 ¹
All patients' have the attitude that the PT should follow exactly what is written on the referral card	21	20.7	0.867
A large proportion of our patients from Mediterranean cultures "hurt everywhere" (and nowhere very specifically), compared to other cultures who are much more precise with the site of their pain	39.5	10.3	0.092
The type of job the patient has (whether he works in the private or public sector) seems to be important in terms of the amount of "sick leave" taken for episodes of LBP	81.5	34.5	< 0.001 ²
I feel patients have a very "passive" attitude regarding physiotherapy treatment	37.8	44.8	0.407
There is a poor understanding among patients about what physiotherapy is and what it entails	57.7	34.5	0.066
There a difference in concordance between rural and urban LBP patients	50.5	65.5	0.476
Diagnostic issues			
Diagnosis in a medical privilege exclusively and doesn't form part of physiotherapy at all	90.9	17.2	< 0.001 ²
I believe diagnosing a condition should be part of physiotherapy practice	90.9	10.3	< 0.001 ²
Formal assessment of the patient prior to commencement of treatment is not performed by a large number of PTs	75.6	89.7	0.441
I believe more emphasis should be given in assessment at undergraduate level than in treatment techniques	92.7	6.9	< 0.001 ²
Performing an X-ray on a patient with LBP is obligatory	57	72.4	0.291
Legally, physiotherapists are "executors" and they cannot interfere greatly in treatment planning (alter it)	40.3	0	0.002 ¹
In general there is an overuse of medical investigations	60.9	3.4	< 0.001 ²
In general there is more emphasis on laboratory investigations at the expense of the clinical investigations	77.4	58.6	0.024 ¹

¹ χ^2 test is statistically significant at the 0.05 level; ² χ^2 test is statistically significant at the 0.001 level. PT: Physiotherapist; LBP: Low back pain; X-ray: Radiograph.

tion focussed only on the biomedical dimension of the patient's problem, indicating that both countries take into consideration the patient's psychosocial status in their assessment. Despite evidence that biomedically orientated diagnostic practice^[49-51] is still the dominant paradigm^[30,52], it is worth noting the adherence that most of these statements (relating to history taking) have with current guideline practice for LBP^[53,54]. It is also interesting to note that psychosocial features were considered important prognostic indicators in LBP recovery and management by both groups^[55-57].

Two statements from the assessment section

highlighted significant differences between populations. Whilst the majority of the British PTs stated that they pay attention to the doctor's medical diagnosis and referral card, most Greek PTs did not seem to agree. This low agreement in the Greek cohort conforms with what was noted during the focus group discussions, in that little credence is afforded to the doctors' medical diagnosis and subsequent referral card^[41].

In terms of re-assessment procedures the majority of the British PTs re-assess within each treatment session (*i.e.*, test-retest following an interventional procedure) as well as following each treatment session whereas, Greek

PTs re-assess following 4-5 treatment sessions. This could reflect the lack of autonomy in decision-making that has been prevalent in Greece for many years.

Patients' attitudes towards assessment

Interestingly, over half of the Greek PTs agreed that following several treatment sessions they start to acknowledge the patients' psychosocial problems. However their British counterparts did not agree with that. This Greek "perspective" is in agreement with the longer gap between re-evaluations (4-5 treatment sessions, as previously indicated) compared to only one for the British PTs, and could possibly imply a longer term management plan and a slower recovery expectation rate compared to the British ones.

Both PT groups disagreed that patients have a passive attitude towards physiotherapy, thus agreeing with a recent British study exploring patients' attitudes and beliefs following physiotherapy, which reported that active patient involvement with their LBP problem was considered essential^[58]. It is interesting to note that over half of the Greek PTs believe that patients have a poor understanding of the role of physiotherapy, compared to only a third of the British PTs, which could reflect the more medically-orientated status existing within Greece. There was also significant disagreement between the PT groups about the association of the working sector with sick leave; Greek PTs agreed that the amount of sick leave a patient takes is associated with his working sector (public or private) compared to a lower agreement range by the British PTs. This could reflect differences in security of employment for the different sectors; *i.e.*, as the Greek public sector entails mostly permanent contracting employees, it could be the case that sick leave can more easily be asked for. However, this is conjecture.

Diagnostic issues

This final section demonstrated with the largest differences between the PT groups (6 out of 8 statements yielded statistically significant results). Most British PTs did not agree with the "Greek notion" that diagnosis is considered a medical privilege and does not form part of physiotherapy. This is to be expected considering that the healthcare infrastructure in Great Britain has moved away from a medically-centred model of care and has adopted a more multidisciplinary approach^[11,18]. Something similar however, has not been detected within Greece yet^[4,8,41]; in Greece medical referrals, dictating (by the doctor) which particular method should the PT follow, are obligatory prior to seeing a physiotherapist and it is anticipated that the PT will follow the exact referral (treatment instructions). Furthermore, 40.3% of the Greek PTs as opposed to none of the British PTs still consider themselves as "executers", not being able to interfere with treatment planning. This barrier to autonomous practice and diagnosis has not been reported in other cultural settings^[23,59,60], probably because autonomy within physiotherapy is not an issue in other developed countries.

Over 90% of the Greek PTs (compared to less than 11% of United Kingdom ones) felt strongly that physiotherapy assessment should be more actively included in undergraduate physiotherapy programmes and diagnosis should also form an official part of physiotherapy practice. The British sample did not agree that there is an overuse of medical investigations in clinical practice in their country. This again, reflects their current guideline practice^[30,61]. Based on the focus group data^[41], X-rays in Greece are used as a means of reassuring and helping patients to recover as well as building upon the doctor-patient relationship. Interestingly, patient reassurance^[62,63], perceived recovery^[34] and enhancement of doctor-patient relationships^[63] were reasons for ordering an X-ray in other cultural settings.

In terms of this study's clinical implications, this cross-cultural report appeared to be beneficial in clarifying commonalities and differences in perspectives and diagnostic practice in LBP between Greek and British PTs. Of particular interest is the fact that both cultural groups appeared to agree on the importance of clinical and psychosocial features during the examination (for targeting treatment), thus, indicating that LBP is a clinical entity whose "somatic expressions" amongst health professionals and patients are common even across different cultural groups. Similarities across the methods utilised in history taking and in the way PTs feel patients perceive physiotherapy practice, also indicate that LBP clinical diagnosis is similar in approach, beyond each country's borders.

However, a number of differences were detected particularly in diagnostic issues raised, such as the utilisation of radiology. Additionally, of the items identified that were culturally distinct these related more to re-assessment procedures and diagnostic practice issues, possibly highlighting the multi-disciplinary approach of the British healthcare system compared to a more unimodal and medically-centred one of the Greek system (*i.e.*, over utilisation of medical investigations, PTs seen as "executers", *etc.*).

However, in view of the qualitative nature of this study and the relatively smaller British sample, these findings cannot be generalised beyond the samples and cultural groups utilised until further work is undertaken. To the authors' knowledge, this is the only study exploring such perspectives and issues relating to LBP practice in two different cultural contexts, and it is believed that these findings in their wider sense reflect cultural variables which may contribute to the understanding of the course and/or management of a given clinical entity in these two countries.

In conclusion, this study aimed to explore current diagnostic practice and attitudes of Greek and United Kingdom physiotherapists on assessing LBP patients *via* a structured questionnaire-type survey. A number of similarities were detected predominantly in history taking methods and in the way patients seem to perceive physiotherapy practice thus, indicating that LBP is similar in approach across different cultural groups. However,

several differences were apparent, particularly in re-assessment procedures as well as in general diagnostic issues regarding the value of the medical diagnosis, overuse of medical investigations, autonomy within physiotherapists, *etc.* These differences may reflect the different evolutionary stages in the healthcare delivery service provided across the two cultural settings; from the more unimodal and medically-centred Greek healthcare system to a more holistic and multi-modal British one.

COMMENTS

Background

It is suggested that cultural differences amongst healthcare professionals: (1) in diagnostic practice of low back pain (LBP); and (2) in terms of attitudes towards their patients care and clinical decision-making tend to "shape" particular attitudes, beliefs and perspectives, which subsequently, have an effect on their overall LBP management approach.

Research frontiers

This study's research hotspots are to compare the current diagnostic practice and the associated attitudes of Greek and United Kingdom physiotherapists on assessing LBP patients.

Innovations and breakthroughs

In terms of conducting the LBP assessment (history taking procedures, *etc.*) both cultural groups presented with similarities, indicating that LBP is similar in approach across the two physiotherapy (PT) cultural groups. It was interesting to note that general diagnostic issues regarding the value of the medical diagnosis, overuse of medical investigations as well as autonomy within physiotherapists, *etc.*, were different, possibly reflecting different evolutionary stages in the healthcare delivery service provided across the two cultural settings (from the more unimodal and medically-centred Greek healthcare system to a more holistic and multi-modal British one).

Applications

This cross-cultural report appeared to be beneficial in clarifying commonalities and differences in perspectives and diagnostic practice in LBP between Greek and British PTs. Similarities indicate that LBP clinical diagnosis is similar in approach, beyond each country's borders. Culturally distinct themes (which related more to re-diagnostic practice issues), possibly highlight the multi-disciplinary approach of the British healthcare system compared to a more unimodal and medically-centred Greek one.

Terminology

LBP refers to any pain in the back region, between the lower rib and the gluteal folds. It is one of the most highly prevalent musculoskeletal disorders with extremely high recurrent rates. In most LBP episodes, a specific underlying cause is not accurately identified and quite often the impact of psychosocial factors (instead of mechanical ones) is believed to be of great importance. As a result, the health professionals' perspectives are important in enhancing or contributing to the management of the patients' psychosocial profile.

Peer-review

In this manuscript, the authors conducted a cross-cultural survey to observe current diagnostic practice and attitudes of Greek and United Kingdom physiotherapists (PTs) on assessing low back pain (LBP) patients. Author's conclusions were that although similarities on history taking methods were detected across both Greek and United Kingdom groups, gross differences were found in re-assessment procedures and diagnostic issues between Greek and British physiotherapists. This topic is small, but informative one for those who are involved in this area.

REFERENCES

1 **Polyzos NM.** Striving towards efficiency in the Greek hospitals by

- reviewing case mix classifications. *Health Policy* 2002; **61**: 305-328 [PMID: 12098523 DOI: 10.1016/S0168-8510(01)00181-6]
- 2 **Marinos G,** Giannopoulos A, Vlasis K, Michail O, Katsargyris A, Gerasimos S, Elias G, Klonaris C, Griniatsos J, Stefanos P, Vasileiou I. Primary care in the management of common orthopaedic problems. *Qual Prim Care* 2008; **16**: 345-349 [PMID: 18973716 DOI: 10.1097/SMJ.0b013e3181826e97]
- 3 **Andrianakos A,** Trontzas P, Christoyannis F, Dantis P, Voudouris C, Georgountzos A, Kaziolas G, Vafiadou E, Pantelidou K, Karamitsos D, Kontelis L, Krachtis P, Nikolia Z, Kaskani E, Tavaniotou E, Antoniadis C, Karanikolas G, Kontoyanni A. Prevalence of rheumatic diseases in Greece: a cross-sectional population based epidemiological study. The ESORDIG Study. *J Rheumatol* 2003; **30**: 1589-1601 [PMID: 12858464]
- 4 **Stranjalis G,** Tsamandouraki K, Sakas DE, Alamanos Y. Low back pain in a representative sample of Greek population: analysis according to personal and socioeconomic characteristics. *Spine (Phila Pa 1976)* 2004; **29**: 1355-1360; discussion 1361 [PMID: 15187638 DOI: 10.1097/01.BRS.00040127181.59012.1C]
- 5 **Antonopoulou M,** Antonakis N, Hadjipavlou A, Lionis C. Patterns of pain and consulting behaviour in patients with musculoskeletal disorders in rural Crete, Greece. *Fam Pract* 2007; **24**: 209-216 [PMID: 17504775 DOI: 10.1093/fampra/cmm012]
- 6 **Vasiliadou A,** Karvountzis GG, Soumilas A, Roumeliotis D, Theodosopoulou E. Occupational low-back pain in nursing staff in a Greek hospital. *J Adv Nurs* 1995; **21**: 125-130 [PMID: 7897063 DOI: 10.1046/j.1365-2648.1995.21010125.x]
- 7 **Alexopoulos EC,** Burdorf A, Kalokerinou A. A comparative analysis on musculoskeletal disorders between Greek and Dutch nursing personnel. *Int Arch Occup Environ Health* 2006; **79**: 82-88 [PMID: 16133523 DOI: 10.1007/s00420-005-0033-z]
- 8 **Alexopoulos EC,** Stathi IC, Charizani F. Prevalence of musculoskeletal disorders in dentists. *BMC Musculoskelet Disord* 2004; **5**: 16 [PMID: 15189564 DOI: 10.1186/1471-2474-5-16]
- 9 **Alexopoulos EC,** Burdorf A, Kalokerinou A. Risk factors for musculoskeletal disorders among nursing personnel in Greek hospitals. *Int Arch Occup Environ Health* 2003; **76**: 289-294 [PMID: 12739172]
- 10 **Spyropoulos P,** Papatthanasiou G, Georgoudis G, Chronopoulos E, Koutis H, Koumoutsou F. Prevalence of low back pain in greek public office workers. *Pain Physician* 2007; **10**: 651-659 [PMID: 17876361]
- 11 **Hillman M,** Wright A, Rajaratnam G, Tennant A, Chamberlain MA. Prevalence of low back pain in the community: implications for service provision in Bradford, UK. *J Epidemiol Community Health* 1996; **50**: 347-352 [PMID: 8935469 DOI: 10.1136/jech.50.3.347]
- 12 **Papageorgiou AC,** Croft PR, Ferry S, Jayson MI, Silman AJ. Estimating the prevalence of low back pain in the general population. Evidence from the South Manchester Back Pain Survey. *Spine (Phila Pa 1976)* 1995; **20**: 1889-1894 [PMID: 8560337 DOI: 10.1097/00007632-199509000-00009]
- 13 **Waxman R,** Tennant A, Helliwell P. Community survey of factors associated with consultation for low back pain. *BMJ* 1998; **317**: 1564-1567 [PMID: 9836660 DOI: 10.1136/bmj.317.7172.1564]
- 14 **Walsh K,** Cruddas M, Coggon D. Low back pain in eight areas of Britain. *J Epidemiol Community Health* 1992; **46**: 227-230 [PMID: 1386619 DOI: 10.1136/jech.46.3.227]
- 15 **Raspe H,** Matthis C, Croft P, O'Neill T. Variation in back pain between countries: the example of Britain and Germany. *Spine (Phila Pa 1976)* 2004; **29**: 1017-1021; discussion 1021 [PMID: 15105675]
- 16 **Waxman R,** Tennant A, Helliwell P. A prospective follow-up study of low back pain in the community. *Spine (Phila Pa 1976)* 2000; **25**: 2085-2090 [PMID: 10954640 DOI: 10.1097/00007632-200008150-00013]
- 17 **Croft PR,** Dunn KM, Raspe H. Course and prognosis of back pain in primary care: the epidemiological perspective. *Pain* 2006; **122**: 1-3 [PMID: 16530969 DOI: 10.1016/j.pain.2006.01.023]
- 18 **Liu JL,** Maniadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. *Heart* 2002; **88**: 597-603 [PMID: 12433888 DOI: 10.1016/S0304-3959(99)00187-6]
- 19 **Deyo RA,** Tsui-Wu YJ. Descriptive epidemiology of low-back pain

- and its related medical care in the United States. *Spine* (Phila Pa 1976) 1987; **12**: 264-268 [PMID: 2954221 DOI: 10.1097/00007632-198704000-00013]
- 20 **Shekelle PG**, Markovich M, Louie R. An epidemiologic study of episodes of back pain care. *Spine* (Phila Pa 1976) 1995; **20**: 1668-1673 [PMID: 7482015 DOI: 10.1097/00007632-199508000-00004]
 - 21 **Atlas SJ**, Deyo RA. Evaluating and managing acute low back pain in the primary care setting. *J Gen Intern Med* 2001; **16**: 120-131 [PMID: 11251764 DOI: 10.1111/j.1525-1497.2001.91141.x]
 - 22 **Cherkin D**, Kovacs FM, Croft P, Borkan J, Foster NE, Oberg B, Urrútia G, Zamora J. The Ninth International Forum for Primary Care Research on Low Back Pain. *Spine* (Phila Pa 1976) 2009; **34**: 304-307 [PMID: 19148040 DOI: 10.1097/BRS.0b013e3181928f9a]
 - 23 **Spoto MM**, Collins J. Physiotherapy diagnosis in clinical practice: a survey of orthopaedic certified specialists in the USA. *Physiother Res Int* 2008; **13**: 31-41 [PMID: 18189334 DOI: 10.1002/pri.390]
 - 24 **Fullen BM**, Baxter GD, O'Donovan BG, Doody C, Daly LE, Hurley DA. Factors impacting on doctors' management of acute low back pain: a systematic review. *Eur J Pain* 2009; **13**: 908-914 [PMID: 19110456 DOI: 10.1016/j.ejpain.2008.11.013]
 - 25 **Fullen BM**, Doody C, David Baxter G, Daly LE, Hurley DA. Chronic low back pain: non-clinical factors impacting on management by Irish doctors. *Ir J Med Sci* 2008; **177**: 257-263 [PMID: 18584269 DOI: 10.1007/s11845-008-0174-7]
 - 26 **Fullen BM**, Baxter GD, O'Donovan BG, Doody C, Daly L, Hurley DA. Doctors' attitudes and beliefs regarding acute low back pain management: A systematic review. *Pain* 2008; **136**: 388-396 [PMID: 18395982 DOI: 10.1016/j.pain.2008.01.003]
 - 27 **Perreault K**, Dionne CE. Patient-physiotherapist agreement in low back pain. *J Pain* 2005; **6**: 817-828 [PMID: 16326370 DOI: 10.1016/j.jpain.2005.07.008]
 - 28 **Haldorsen EM**, Brage S, Johannesen TS, Tellnes G, Ursin H. Musculoskeletal pain: concepts of disease, illness, and sickness certification in health professionals in Norway. *Scand J Rheumatol* 1996; **25**: 224-232 [PMID: 8792799 DOI: 10.3109/03009749609069991]
 - 29 **Linton SJ**, Vlaeyen J, Ostelo R. The back pain beliefs of health care providers: are we fear-avoidant? *J Occup Rehabil* 2002; **12**: 223-232 [PMID: 12389475 DOI: 10.1023/A: 1020218422974]
 - 30 **Bishop A**, Foster NE, Thomas E, Hay EM. How does the self-reported clinical management of patients with low back pain relate to the attitudes and beliefs of health care practitioners? A survey of UK general practitioners and physiotherapists. *Pain* 2008; **135**: 187-195 [PMID: 18206309 DOI: 10.1016/j.pain.2007.11.010]
 - 31 **Schers H**, Braspenning J, Drijver R, Wensing M, Grol R. Low back pain in general practice: reported management and reasons for not adhering to the guidelines in The Netherlands. *Br J Gen Pract* 2000; **50**: 640-644 [PMID: 11042916]
 - 32 **Negrini S**, Politano E, Carabalona R, Mambrini A. General practitioners' management of low back pain: impact of clinical guidelines in a non-English-speaking country. *Spine* (Phila Pa 1976) 2001; **26**: 2727-2733; discussion 2734 [PMID: 11740363 DOI: 10.1097/00007632-200112150-00021]
 - 33 **Szpalski M**, Nordin M, Skovron ML, Melot C, Cukier D. Health care utilization for low back pain in Belgium. Influence of socio-cultural factors and health beliefs. *Spine* (Phila Pa 1976) 1995; **20**: 431-442 [PMID: 7747226 DOI: 10.1097/00007632-199502001-00005]
 - 34 **Espeland A**, Baerheim A. Factors affecting general practitioners' decisions about plain radiography for back pain: implications for classification of guideline barriers—a qualitative study. *BMC Health Serv Res* 2003; **3**: 8 [PMID: 12659640 DOI: 10.1186/1472-6963-3-8]
 - 35 **Ammendolia C**, Bombardier C, Hogg-Johnson S, Glazier R. Views on radiography use for patients with acute low back pain among chiropractors in an Ontario community. *J Manipulative Physiol Ther* 2002; **25**: 511-520 [PMID: 12381973 DOI: 10.1067/mmt.2002.127075]
 - 36 **Margarido Mdo S**, Kowalski SC, Natour J, Ferraz MB. Acute low back pain: diagnostic and therapeutic practices reported by Brazilian rheumatologists. *Spine* (Phila Pa 1976) 2005; **30**: 567-571 [PMID: 15738792 DOI: 10.1097/01.brs.0000154690.04674.06]
 - 37 **Selim AJ**, Fincke G, Ren XS, Deyo RA, Lee A, Skinner K, Kazis L. Racial differences in the use of lumbar spine radiographs: results from the Veterans Health Study. *Spine* (Phila Pa 1976) 2001; **26**: 1364-1369 [PMID: 11426153 DOI: 10.1097/00007632-200106150-00021]
 - 38 **Skelton AM**, Murphy EA, Murphy RJ, O'Dowd TC. General practitioner perceptions of low back pain patients. *Fam Pract* 1995; **12**: 44-48 [PMID: 7665040 DOI: 10.1093/fampra/12.1.44]
 - 39 **Coudeyre E**, Tubach F, Rannou F, Baron G, Coriat F, Brin S, Revel M, Poiraudou S. Fear-avoidance beliefs about back pain in patients with acute LBP. *Clin J Pain* 2007; **23**: 720-725 [PMID: 17885352 DOI: 10.1097/AJP.0b013e31814da407]
 - 40 **Sanders SH**, Brena SF, Spier CJ, Beltrutti D, McConnell H, Quintero O. Chronic low back pain patients around the world: cross-cultural similarities and differences. *Clin J Pain* 1992; **8**: 317-323 [PMID: 1493342 DOI: 10.1097/00002508-199212000-00006]
 - 41 **Billis EV**, McCarthy CJ, Stathopoulos I, Kapreli E, Pantzou P, Oldham JA. The clinical and cultural factors in classifying low back pain patients within Greece: a qualitative exploration of Greek health professionals. *J Eval Clin Pract* 2007; **13**: 337-345 [PMID: 17518796 DOI: 10.1111/j.1365-2753.2006.00698.x]
 - 42 **McCarthy CJ**, Rushton A, Billis V, Arnall F, Oldham JA. Development of a clinical examination in non-specific low back pain: a Delphi technique. *J Rehabil Med* 2006; **38**: 263-267 [PMID: 16801210 DOI: 10.1080/16501970600632768]
 - 43 **Hasson F**, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs* 2000; **32**: 1008-1015 [PMID: 11095242]
 - 44 **Keeney S**, Hasson F, McKenna H. Consulting the oracle: ten lessons from using the Delphi technique in nursing research. *J Adv Nurs* 2006; **53**: 205-212 [PMID: 16422719 DOI: 10.1111/j.1365-2648.2006.03716.x]
 - 45 **Ferguson FC**, Brownlee M, Webster V. A Delphi study investigating consensus among expert physiotherapists in relation to the management of low back pain. *Musculoskeletal Care* 2008; **6**: 197-210 [PMID: 18311847 DOI: 10.1002/msc.126]
 - 46 **Oswald AE**, Bell MJ, Snell L, Wiseman J. The current state of musculoskeletal clinical skills teaching for preclerkship medical students. *J Rheumatol* 2008; **35**: 2419-2426 [PMID: 18925682 DOI: 10.3899/jrheum.080308]
 - 47 **Wolf JM**, Ritter M, Weiss AP, Akelman E. Access and use of the internet in a hand surgery population. *Hand Surg* 2004; **9**: 29-33 [PMID: 15368622 DOI: 10.1142/S0218810404002121]
 - 48 **Raikin SM**, Bley LA, Leb RB. Emerging technology: remote analysis of traumatic musculoskeletal radiographs transmitted by electronic mail. *J Orthop Trauma* 1999; **13**: 516-519 [PMID: 10513978 DOI: 10.1097/00005131-199909000-00012]
 - 49 **Sieben JM**, Vlaeyen JW, Portegijs PJ, Warmenhoven FC, Sint AG, Dautzenberg N, Romeijnders A, Arntz A, Knottnerus JA. General practitioners' treatment orientations towards low back pain: influence on treatment behaviour and patient outcome. *Eur J Pain* 2009; **13**: 412-418 [PMID: 18562224 DOI: 10.1016/j.ejpain.2008.05.002]
 - 50 **Miller JS**, Pinnington MA. Straightforward consultation or complicated condition? General practitioners' perceptions of low back pain. *Eur J Gen Pract* 2003; **9**: 3-9 [PMID: 14611007 DOI: 10.3109/13814780309160385]
 - 51 **Kent P**, Keating JL. Classification in nonspecific low back pain: what methods do primary care clinicians currently use? *Spine* (Phila Pa 1976) 2005; **30**: 1433-1440 [PMID: 15959374 DOI: 10.1097/01.brs.0000166523.84016.4b]
 - 52 **Coudeyre E**, Rannou F, Tubach F, Baron G, Coriat F, Brin S, Revel M, Poiraudou S. General practitioners' fear-avoidance beliefs influence their management of patients with low back pain. *Pain* 2006; **124**: 330-337 [PMID: 16750297 DOI: 10.1016/j.pain.2006.05.003]
 - 53 **van Tulder M**, Becker A, Bekkering T, Breen A, del Real MT, Hutchinson A, Koes B, Laerum E, Malmivaara A. Chapter 3. European guidelines for the management of acute nonspecific low back pain in primary care. *Eur Spine J* 2006; **15** Suppl 2:

- S169-S191 [PMID: 16550447]
- 54 **Koes BW**, van Tulder MW, Ostelo R, Kim Burton A, Waddell G. Clinical guidelines for the management of low back pain in primary care: an international comparison. *Spine* (Phila Pa 1976) 2001; **26**: 2504-2513; discussion 2513-2514 [PMID: 11707719 DOI: 10.1097/00007632-200111150-00022]
- 55 **Burton AK**, Tillotson KM, Main CJ, Hollis S. Psychosocial predictors of outcome in acute and subchronic low back trouble. *Spine* (Phila Pa 1976) 1995; **20**: 722-728 [PMID: 7604349 DOI: 10.1097/00007632-199503150-00014]
- 56 **Buer N**, Linton SJ. Fear-avoidance beliefs and catastrophizing: occurrence and risk factor in back pain and ADL in the general population. *Pain* 2002; **99**: 485-491 [PMID: 12406524 DOI: 10.1016/S0304-3959(02)00265-8]
- 57 **van der Windt DA**, Kuijpers T, Jellema P, van der Heijden GJ, Bouter LM. Do psychological factors predict outcome in both low-back pain and shoulder pain? *Ann Rheum Dis* 2007; **66**: 313-319 [PMID: 16916857 DOI: 10.1136/ard.2006.053553]
- 58 **May S**. Patients' attitudes and beliefs about back pain and its management after physiotherapy for low back pain. *Physiother Res Int* 2007; **12**: 126-135 [PMID: 17624898 DOI: 10.1002/pri.367]
- 59 **Sherman KJ**, Cherkin DC, Deyo RA, Erro JH, Hrbek A, Davis RB, Eisenberg DM. The diagnosis and treatment of chronic back pain by acupuncturists, chiropractors, and massage therapists. *Clin J Pain* 2006; **22**: 227-234 [PMID: 16514321 DOI: 10.1097/01.ajp.0000169668.62900.ca]
- 60 **Bogefeldt J**, Grunnesjö M, Svärdsudd K, Blomberg S. Diagnostic differences between general practitioners and orthopaedic surgeons in low back pain patients. *Ups J Med Sci* 2007; **112**: 199-212 [PMID: 17578820 DOI: 10.3109/2000-1967-194]
- 61 **CSAG**. Clinical Standards Advisory Group on Back Pain. "Back Pain. Report of a CSAG Committee on Back Pain", 1994. ISBN 0-11-321887-7
- 62 **Little P**, Cantrell T, Roberts L, Chapman J, Langridge J, Pickering R. Why do GPs perform investigations? The medical and social agendas in arranging back X-rays. *Fam Pract* 1998; **15**: 264-265 [PMID: 9694186 DOI: 10.1093/fampra/15.3.264]
- 63 **Baker R**, Lecouturier J, Bond S. Explaining variation in GP referral rates for x-rays for back pain. *Implement Sci* 2006; **1**: 15 [PMID: 16884536 DOI: 10.1186/1748-5908-1-15]

P- Reviewer: Lykissas MG, Peng BG, Sakkas LI, Shin BC, Whiteside D

S- Editor: Qiu S **L- Editor:** A **E- Editor:** Li D



Observational Study

Epidemiology of isolated hand injuries in the United Arab Emirates

Michal Grivna, Hani O Eid, Fikri M Abu-Zidan

Michal Grivna, Institute of Public Health, College of Medicine and Health Sciences, UAE University, PO Box 17666, Al Ain, United Arab Emirates

Hani O Eid, Fikri M Abu-Zidan, Department of Surgery, College of Medicine and Health Sciences, UAE University, PO Box 17666, Al Ain, United Arab Emirates

Fikri M Abu-Zidan, Department of Surgery, Al Ain Hospital, PO Box 17666, Al Ain, United Arab Emirates

Author contributions: Grivna M, Eid HO and Abu-Zidan FM conceived and designed the experiments, analyzed the data, contributed reagents/materials/analysis tools, critically read the paper and approved final version; Grivna M and Abu-Zidan FM wrote the paper; Eid HO performed the experiments.

Supported by An Interdisciplinary UAE University grant, No. 02-07-8-1/4.

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of Al Ain Health District (UAE RECA/02/44).

Informed consent statement: All study participants, or their legal guardian, provided written consent prior to study enrolment.

Conflict-of-interest statement: The authors of this manuscript have no conflicts of interest to disclose.

Data sharing statement: There is no additional data available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Fikri M Abu-Zidan, MD, FACS, FRCS, PhD, DipApplStats, Professor, Department of Surgery, College of Medicine and Health Sciences, UAE University, PO Box 17666, Al Ain, United Arab Emirates. fabuzidan@uaeu.ac.ae
Telephone: +971-3-7137579
Fax: +971-3-7672067

Received: March 6, 2016

Peer-review started: March 7, 2016

First decision: May 16, 2016

Revised: May 29, 2016

Accepted: June 27, 2016

Article in press: June 29, 2016

Published online: September 18, 2016

Abstract

AIM

To provide suggestions for hand injury prevention by study the demography and risk factors of casualties suffering from isolated hand injuries.

METHODS

All trauma patients with isolated hand injuries who were admitted to Al Ain Hospital for more than 24 h during a period of 3 years were studied. Patient demographics, location, mechanism/time of injury, and length of hospital stay were all analyzed.

RESULTS

Two hundred and ten patients were studied. Their mean age was 29.7 years. Males constituted 92%. Sixty-five point one percent of all cases were from the Indian subcontinent. The workplace was the most common location of injury (67.1%), followed by the home (17.1%) and road (6.2%). Machinery caused 36.2% of all injuries, followed by heavy object (20.5%) and fall (11%). Cases injured at home were young ($P < 0.0001$) with an associated higher incidence of females ($P < 0.0001$).

CONCLUSION

Male workers in Al Ain city are at greater risk of sustaining hand injuries, predominantly from machinery. Safety education, personal protection, and the enforcement of safety standards are essential to the prevention and avoidance of hand injury.

Key words: United Arab Emirates; Occupational safety; Hand injury; Injury prevention

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Two hundred and ten hospitalized patients with isolated hand injuries were prospectively studied in Al Ain Hospital, United Arab Emirates. Males were in greater danger of sustaining work-related hand injuries especially from machinery. Safety education, personal protection, and enforcement of safety standards are essential for hand injury prevention.

Grivna M, Eid HO, Abu-Zidan FM. Epidemiology of isolated hand injuries in the United Arab Emirates. *World J Orthop* 2016; 7(9): 570-576 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/570.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.570>

INTRODUCTION

Hand injuries are common in young men^[1,2]. They constitute 7%-28% of all injuries^[3,4], and account for about one fifth of all emergencies presenting to hospital emergency departments^[5]. Although the outcome of hand injuries is seldom fatal, patients may suffer substantial disability^[6]. Types of injuries vary from soft tissue injuries and lacerations to burns, fractures, and amputations^[7]. The costs of treatment are high as some patients may require hand reconstruction^[7]. Many of these injuries affect the dominant hand^[8] and can cause considerable physical disability and psychological stress^[9,10].

The United Arab Emirates (UAE) is a country experiencing a rapid economic development. The population, reportedly circa 4 million in 2003, consisted of a high proportion of expatriate workers^[11]. Injury remains the second main cause of fatalities at 27.3 per 100000 persons per year^[12]. Data on isolated hand injuries are lacking in this region. There is a need for information on risk factors for hand injuries related to the individual, the environment and the equipment in order to allow the development of efficient injury prevention and safety promotion^[12]. To reduce the effect of associated injuries it was decided to study only patients with isolated hand injuries who had been admitted to Al Ain hospital.

The purpose of the study was to evaluate the risk factors of inpatients with isolated hand injuries so that recommendations for hand injury prevention in the UAE could be advocated.

MATERIALS AND METHODS

Ethical approval

Ethical approval for this study was obtained from Al Ain Health District Ethics Committee (ethical approval No: RECA/02/44). All patients who are admitted to Al Ain Hospital, or their legal guardian, sign a general consent form permitting the use of their anonymous data for audit and research.

Data collection and setting

Data of all patients with isolated hand injuries and who were hospitalized more than 24 h were retrieved from Al Ain Hospital Trauma Registry. During a 36-mo period (March 2003-March 2006), data from the Registry were prospectively collected by a full time Trauma Research Fellow. Al Ain Hospital is a major specialized acute care hospital with a capacity of more than 400 beds^[13]. The hospital cared for approximately 80% of trauma cases in Al Ain during the study period. The hospital is located in Al Ain City which had a population of 460000 during that period. Twenty-two percent of cases were UAE nationals while the remainder came from the expatriate work force^[11]. Nationalities were categorized as Indian subcontinent and others as it had been previously shown that risks of injury for these two groups in Al Ain differed. There is a significantly higher proportion of manual laborers in Al Ain from the Indian subcontinent^[14,15].

Studied variables included gender, age, nationality, mechanism and anatomical location of hand injury, time/date of injury, and length of hospital stay.

Calculations and statistics

We used Kruskal Wallis test to compare continuous and ordinal data and Fisher's exact test to compare categorical data. A *P*-value of less than 0.05 was considered significant. Data were analyzed using Statistical Package for the Social Sciences (IBM-SPSS version 21, Chicago, IL, United States).

RESULTS

Out of 2573 patients in the Trauma Registry, 210 patients sustained isolated hand injuries (8.2%). The majority of patients were male (91.9%, *n* = 193). The average (SD) age of cases was 29.7 (12.6) years. There were two peaks, in children < 5 years old injured mostly at home, and younger adults 20-30 years injured at work (Figure 1). Seventy-two point seven percent of patients (*n* = 152) were in the age group of 20-44; children and youth < 20 years constituted 14.7% (*n* = 31) (Figure 1). In respect of nationality, the majority of patients came from India, Pakistan, Bangladesh and Sri Lanka (65.1%, *n* = 136), then other Arabs (21.1%, *n* = 44), UAE nationals (7.6%, *n* = 16) and other nationalities (6.2%, *n* = 13). Patients from the Indian subcontinent were significantly older than UAE-nationals and others (*P* = 0.002).

Machinery and heavy objects caused more than half

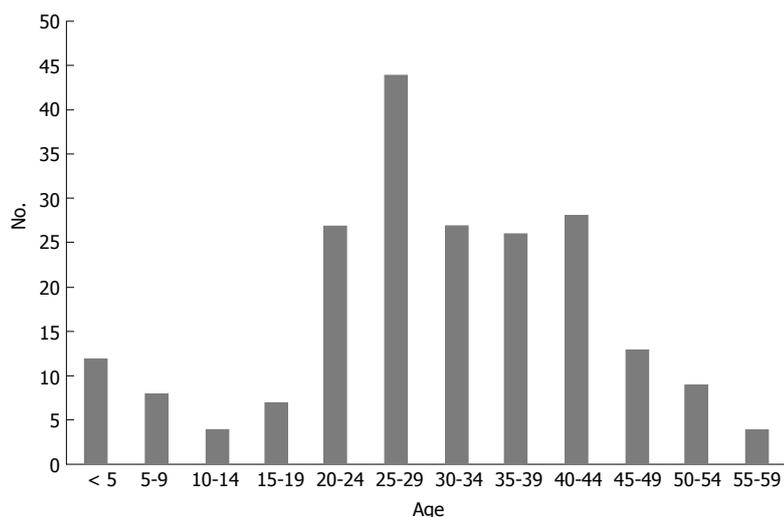


Figure 1 A histogram showing the age distribution of hospitalized patients having isolated hand injuries, Al Ain Hospital, 2003-2006 (n = 210).

Table 1 Isolated hand injury hospitalization by age group and mechanism, Al Ain Hospital, 2003-2006 (n = 210) n (%)

Variable	Age groups			Total
	0-14	15-29	30-59	
Machinery	1 (4.2)	32 (41)	43 (40.2)	76 (36.4)
Heavy object	3 (12.5)	12 (15.4)	28 (26.2)	43 (20.6)
Fall	5 (20.8)	9 (11.5)	9 (8.4)	23 (11)
Cut	6 (25)	9 (11.5)	5 (4.7)	20 (9.6)
Traffic	3 (12.5)	6 (7.7)	7 (6.5)	16 (7.6)
Burn	4 (16.7)	4 (5.1)	7 (6.5)	15 (7.2)
Crush	1 (4.2)	2 (2.6)	2 (1.9)	5 (2.4)
Animal	1 (4.2)	0	3 (2.8)	4 (1.9)
Other	0	4 (5.1)	3 (2.8)	7 (3.3)
Total	24 (100) ¹	78 (100) ¹	107 (100)	209 (100) ¹

¹The percentage may not add to 100 due to rounding; age of 1 patient was unknown.

Table 2 Isolated hand injury hospitalization by location and mechanism, Al Ain Hospital, 2003-2006 (n = 210) n (%)

Variable	Location of injury				Total
	Work	Road	Home	Other	
Machinery	72 (51.1)	0	2 (5.6)	2 (10)	76 (36.2)
Heavy object	39 (27.7)	0	4 (11.1)	0	43 (20.5)
Fall	8 (5.7)	1 (7.7)	9 (25)	5 (25)	23 (11)
Cut	8 (5.7)	0	10 (27.8)	2 (10)	20 (9.5)
Burn	9 (6.4)	0	6 (16.7)	1 (5)	16 (7.6)
Traffic	0	12 (92.3)	1 (2.8)	3 (15)	16 (7.6)
Crush	3 (2.1)	0	2 (5.6)	0	5 (2.4)
Animal	0	0	0	4 (20)	4 (1.9)
Other	2 (1.4)	0	2 (5.6)	3 (15)	7 (3.3)
Total	141 (100) ¹	13 (100)	36 (100) ¹	20 (100)	210 (100) ¹

¹The percentage may not add to 100 due to rounding.

of all injuries (Table 1). Children < 15 years were mainly injured by cuts, followed by falls and burns (Table 1). In the productive age (15-59 years), the most common mechanisms of injury were machinery and heavy object (Table 1). Two injuries were caused by assault (1%),

Table 3 Demography and hospital stay of isolated hand injury by location of injury, Al Ain Hospital, 2003-2006 (n = 210)

Variable	Work n = 141	Road n = 13	Home n = 36	P-value
Age	32 (18-55)	40 (14-45)	11.5 (1-57)	< 0.0001
Gender				
Males	98.6% (139)	100% (13)	61.1% (22)	< 0.0001
Females	1.4% (2)	0	38.9% (14)	
Nationality				
UAE	1.4% (2)	7.7% (1)	27.8% (10)	< 0.0001
Indian Subcontinent	76.6% (108)	46.2% (6)	30.6% (11)	
Others	21.3% (30)	46.2% (6)	41.7% (15)	
Hospital days	6 (1-110)	6 (2-17)	3.5 (2-22)	0.008

Twenty-six patients injured in other locations were not included; Data are presented as median (range) or number (%) as appropriate; P = Kruskal Wallis test or Fisher's Exact test as appropriate. UAE: United Arab Emirates.

and all other were unintentional.

Work was the most common location for isolated hand injury (67.1%), followed by home (17.1%) and road (6.2%) (Table 2). The most common cause of injury at work was machinery (51.1%) followed by heavy object (27.7%); while at home it was cuts (27.8%) followed by fall (25%) and burn (16.7%) (Table 2). Home cases were significantly younger (P < 0.0001) (Table 3). More males than females were significantly injured at work and road (P < 0.0001) (Table 3). More females than males sustained injury at home (P < 0.0001) (Table 3). Nationals from the Indian subcontinent were more often injured at work (76.6%), while UAE nationals were more often injured at home (27.8%) (Table 3).

During the day there were three peaks: In the morning at around 9 o'clock, at lunch time at around noon, in the evening at around 5 o'clock (Figure 2A). During the week, injuries occurred most often on Saturdays, which was, during the study period, the first working day of the week (Figure 2B). There was a peak of injuries during

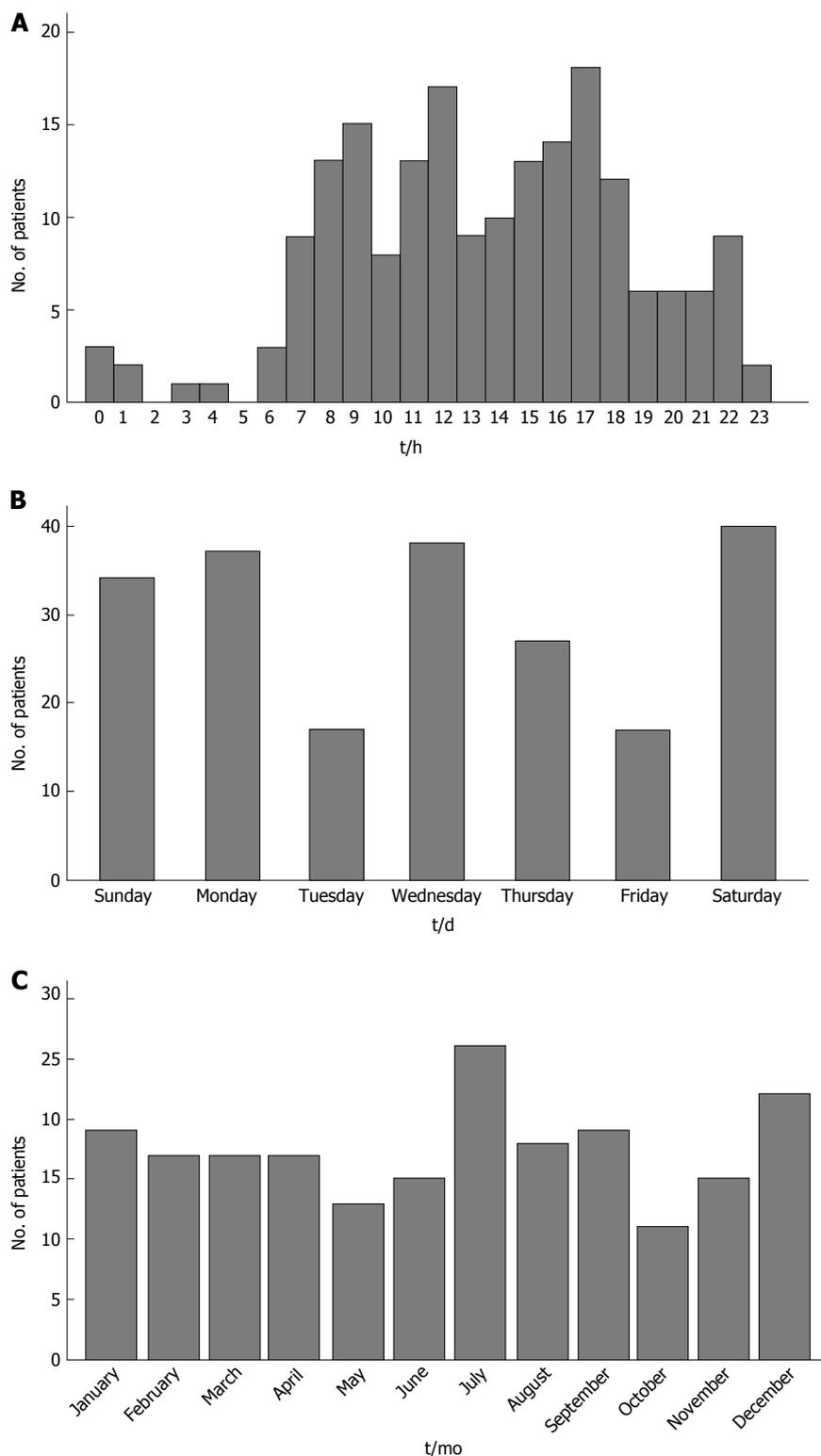


Figure 2 Distribution of hospitalized patients having isolated hand injuries by the hour of the day (A), day of the week (B), and the month of the year (C), Al Ain Hospital, 2003-2006 (n = 210).

summer in July (Figure 2C).

The length of hospital stay ranged from 1 to 110 d (mean 7.9; median 5). Those who were injured at home had a significantly shorter hospital stay ($P < 0.0001$) (Table 3). Forty-eight/two hundred and ten (22.9%) patients sustained an amputation of one finger or more. There were no deaths of studied patients during the

study period.

DISCUSSION

The highest risk group for hand injuries in our setting was young male adults. Males from the Indian subcontinent were commonly injured at work, while UAE nationals

were more commonly injured at home.

The proportion of hand injuries (8.2%) in all injured patients and the proportion of males (91.9%) in those with hand injuries in our study was higher compared with studies in Sweden, Poland and Nigeria^[1,2,8]. As indicated in other studies, it was found that young males sustained injury mainly at work^[16,17]. Immigrant construction workers, mainly from the Indian subcontinent, were found to be at a higher risk of isolated hand injury^[18]. If injured, workers may lose their employment, income, and jeopardize both their socio-economic status and family life. The majority of women in this study sustained injury at home, where they stay most of their time due to cultural factors. This finding exemplifies the importance of home safety in the UAE setting.

The mean age in our study (29.7 years) was similar to that found in other studies^[16,19]. In this study, 14.7% were children and youth < 20 years. The hand is one of the most commonly injured body regions in children^[20], which may be explained by their lack of appreciation of risk. The majority of pediatric injuries in our study were sustained at home, similar to findings in a recent study in the United States^[21].

Machinery caused the most often hand injury in this study, followed by heavy objects, both of which are common causes of hand injury in industrialized countries^[2,16]. These injuries occur as a result of inattention, tiredness, stress, doing an unusual task, being rushed, and the use of poorly maintained or defective machinery^[10,22]. Hand injuries caused by machinery are usually more severe and can lead to permanent loss of hand function or even amputation^[2]. Adopting the use of gloves can decrease the risk of lacerations and punctures, but not crushing, fractures, avulsions, amputations or dislocations^[23]. Other preventive measures, including engineering control and safety training, are necessary to reduce the incidence of more severe injuries^[23].

Violence-related injuries are uncommon in this community compared to other countries. Violence constituted only 1% in this study. In a report from Nigeria, the high level of violence was associated with a high incidence of gunshot injuries to the hand^[8]. Although the percentage of burns in this study was similar to those in other reports, the burn hazards differed^[8]. It has been previously reported that scalds from hot liquids were the major hazard at home, compared with gas and flames at work^[24]. Sport-related hand injuries were not seen in our study compared with a European study that indicated a high prevalence of these injuries^[25]. It is possible that the majority of people in this community do not participate in outdoor sport activities because of hot weather and long working hours.

Animal-related hand injuries were not common in this study (1.9%), and were mainly caused by camels^[26]. Many farm workers in the UAE take care of camels, a large animal with a powerful, incisive bite^[27].

Twenty-two point nine percent of patients in this study sustained finger amputations, similar to findings in other studies^[8,16]. The identification of the object causing amputation was not possible in this study.

Usually these amputations in adults are caused by press machines and powered wood cutters^[28], and, in children, by doors, furniture, and machinery^[29]. These amputations are particularly devastating to the patients and cause distress due to the physical loss and a need for body image adjustment^[30].

Similar to findings in other studies, it was found that the peak time of injury in the morning was around 9 o'clock^[31]. Workers in the UAE tend to work long hours with an associated reduced time for sleep. It has been reported elsewhere that sleep deprivation decreases alertness, adversely affects work performance and constitutes a serious work hazard^[32].

It was also found that injuries were sustained most often on Saturdays, the first day of work in the UAE after the weekend. The first working day of the week usually had the highest incidence of hand injuries^[19]. Similar to findings in other studies, the incidence of injuries was high during summer. It is possible that hot outdoor temperatures in the UAE cause a decrease in the vigilance of outdoor workers^[19].

Hospital stays of patients with hand injuries are usually longer in the UAE than for other injuries because of the greater need for rehabilitation^[2]. It is believed that the longer hospital stays among those injured at work were the result of the social circumstances of UAE expatriate workers. Many of them live alone and without support in crowded accommodation and so prefer to remain as long as possible in the more congenial and supportive environment of the hospital.

It should be emphasized that this study is an epidemiological study and not a clinical outcome study. Injury prevention remains an important duty of trauma surgeons, whose responsibility it is to define risk factors pertaining to injury, to carry out studies on interventional injury prevention and their effects, and to support health promotion through in-depth research on injury prevention^[33-35].

Limitations

This study has certain limitations that require to be highlighted. Patients with minor hand injuries were managed at the Emergency Department. Those who stayed in the hospital for less than 24 h were not included. The Trauma Registry was based in Al Ain hospital, therefore the results of this study may not be generalized for the whole UAE population. This study was for a limited time which was funded by the National University. It is a unique and important source of data for GCC countries. Although these data are a decade old, we think that they still reflect the present situation as isolated hand injury risk factors have not changed in the working environment during this period. Manual laborers still normally do not wear gloves, the electrical saw machines still usually do not have in-built safety, and safety precautions are still not properly followed by labourers. Finally, some important variables were missing like details of occupation, information about injury of dominant hand, absence of functional outcome, occupational experience, length of working

shifts, the causal activity of the person during the injury (smoking or consumption of alcohol), inadequate training, deployment of safety equipment and protective gear, as well as socio-economic variables. There is a need for additional research on causal factors in hand injuries and the importance of transferring these research findings into safety practice in the UAE.

Isolated hand injuries constitute a major proportion of admitted trauma patients in Al Ain city with lengthy hospital stays. Males are at greater risk of sustaining isolated hand injuries especially at work, the majority from machinery. Safety education, personal protection and the enforcement of safety standards could reduce both the need for hospitalization and the incidence of disability in relation to hand injuries.

ACKNOWLEDGMENTS

John Anthony Barrett, M.Phil., English lecturer helped with the revision of the final draft.

COMMENTS

Background

Hand injuries are common in young men. They rarely lead to death, but may cause serious physical disability and psychological stress. Some may require hand reconstruction with associated high cost of treatment. There is a lack of information on personal, environmental and product/equipment risk factors for hand injuries.

Research frontiers

The aim of the study was to investigate demographics and risk factors of hospitalized patients with isolated hand injuries in order to give recommendations for hand injury prevention.

Innovations and breakthroughs

The majority of patients with isolated hand injuries in this study were males. The most common location was work, followed by home and road. Females were injured more at home. Patients injured at home were younger. The most common mechanism was injury from machinery, followed by heavy object and fall. Children < 15 years were mainly injured by cuts, followed by falls and burns.

Applications

Male workers are in higher risk for isolated hand injury, especially from machinery. Safety education, the use of personal protective equipment, and the proper enforcement of safety guidelines are essential.

Terminology

UAE: United Arab Emirates; GCC: Gulf Cooperation Council is a political and economic union consisting of Arab countries - Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates; IBM-SPSS: Statistical Package for the Social Sciences.

Peer-review

The paper describes an epidemiological study concerning isolated hand injuries supported by solid references. This study is definitely worth publishing.

REFERENCES

- 1 **Rosberg HE**, Carlsson KS, Dahlin LB. Prospective study of patients with injuries to the hand and forearm: costs, function, and general health. *Scand J Plast Reconstr Surg Hand Surg* 2005; **39**: 360-369 [PMID: 16298809 DOI: 10.1080/02844310500340046]
- 2 **Trybus M**, Lorkowski J, Brongel L, Hladki W. Causes and consequences of hand injuries. *Am J Surg* 2006; **192**: 52-57 [PMID: 16769275 DOI: 10.1016/j.amjsurg.2005.10.055]
- 3 **Hill C**, Riaz M, Mozzam A, Brennen MD. A regional audit of hand and wrist injuries. A study of 4873 injuries. *J Hand Surg Br* 1998; **23**: 196-200 [PMID: 9607659 DOI: 10.1016/S0266-7681(98)80174-5]
- 4 **Packer GJ**, Shaheen MA. Patterns of hand fractures and dislocations in a district general hospital. *J Hand Surg Br* 1993; **18**: 511-514 [PMID: 8409670 DOI: 10.1016/0266-7681(93)90161-8]
- 5 **Dias JJ**, Garcia-Elias M. Hand injury costs. *Injury* 2006; **37**: 1071-1077 [PMID: 17045996 DOI: 10.1016/j.injury.2006.07.023]
- 6 **Hart RG**. Hand injury prevention. *Ann Emerg Med* 2005; **45**: 636-638 [PMID: 15940098 DOI: 10.1016/j.annemergmed.2004.12.010]
- 7 **Şahin F**, Akca H, Akkaya N, Zincir ÖD, Işık A. Cost analysis and related factors in patients with traumatic hand injury. *J Hand Surg Eur Vol* 2013; **38**: 673-679 [PMID: 23204134 DOI: 10.1177/1753193412469012]
- 8 **Ihekire O**, Salawu SA, Opadele T. International surgery: causes of hand injuries in a developing country. *Can J Surg* 2010; **53**: 161-166 [PMID: 20507787]
- 9 **Horton TC**, Dias JJ, Burke FD. Social deprivation and hand injury. *J Hand Surg Eur Vol* 2007; **32**: 256-261 [PMID: 17335948 DOI: 10.1016/j.jhsb.2006.10.005]
- 10 **Sorock GS**, Lombardi DA, Courtney TK, Cotnam JP, Mittleman MA. Epidemiology of occupational acute traumatic hand injuries: a literature review. *Safety Science* 2001; **38**: 241-256 [DOI: 10.1016/S0925-7535(01)00004-2]
- 11 **United Arab Emirates Ministry of Economy**. Preliminary results of population, housing and establishment census 2005. United Arab Emirates, 2006: 6
- 12 **Grivna M**, Aw TC, El-Sadig M, Loney T, Sharif AA, Thomsen J, Mauzi M, Abu-Zidan FM. The legal framework and initiatives for promoting safety in the United Arab Emirates. *Int J Inj Contr Saf Promot* 2012; **19**: 278-289 [PMID: 22803840 DOI: 10.1080/17457300.2012.696660]
- 13 Al Ain Hospital website. 2016. Available from: URL: <https://www.seha.ae/alain/English/pages/default.aspx>
- 14 **Grivna M**, Eid HO, Abu-Zidan FM. Epidemiology, morbidity and mortality from fall-related injuries in the United Arab Emirates. *Scand J Trauma Resusc Emerg Med* 2014; **22**: 51 [PMID: 25178823 DOI: 10.1186/s13049-014-0051-5]
- 15 **Grivna M**, Eid HO, Abu-Zidan FM. Injuries from falling objects in the United Arab Emirates. *Int J Inj Contr Saf Promot* 2015; **22**: 68-74 [PMID: 24345025 DOI: 10.1080/17457300.2013.863784]
- 16 **Ahmed E**, Chaka T. Prospective study of patients with hand injury: Tikur Anbessa University Teaching Hospital, Addis Ababa. *Ethiop Med J* 2006; **44**: 175-181 [PMID: 17447381]
- 17 **Mink van der Molen AB**, Ettema AM, Hovius SE. Outcome of hand trauma: the hand injury severity scoring system (HISS) and subsequent impairment and disability. *J Hand Surg Br* 2003; **28**: 295-299 [PMID: 12849937 DOI: 10.1016/S0266-7681(03)00082-2]
- 18 **Al-Dawood KM**. Non-fatal occupational injuries admitted to hospitals among general organization for social insurance workers in Al-khobar city, Saudi Arabia: experience of one year. *J Family Community Med* 2000; **7**: 35-42 [PMID: 23008620]
- 19 **Davas Aksan A**, Durusoy R, Ada S, Kayalar M, Aksu F, Bal E. Epidemiology of injuries treated at a hand and microsurgery hospital. *Acta Orthop Traumatol Turc* 2010; **44**: 352-360 [PMID: 21343685 DOI: 10.3944/AOTT.2010.2372]
- 20 **Fitoussi F**. [Hand injuries in children]. *Chir Main* 2013; **32** Suppl 1: S2-S6 [PMID: 23522978 DOI: 10.1016/j.main.2013.02.017]
- 21 **Shah SS**, Rochette LM, Smith GA. Epidemiology of pediatric hand injuries presenting to United States emergency departments, 1990 to 2009. *J Trauma Acute Care Surg* 2012; **72**: 1688-1694 [PMID: 22695442 DOI: 10.1097/TA.0b013e31824a4c5b]
- 22 **Leixnering M**, Quadlbauer S, Szolarcz C, Schenk C, Leixnering S, Körpert K. [Prevention of hand injuries - current situation in Europe]. *Handchir Mikrochir Plast Chir* 2013; **45**: 339-343 [PMID: 24357478 DOI: 10.1055/s-0033-1358732]

- 23 **Sorock GS**, Lombardi DA, Peng DK, Hauser R, Eisen EA, Herrick RF, Mittleman MA. Glove use and the relative risk of acute hand injury: a case-crossover study. *J Occup Environ Hyg* 2004; **1**: 182-190 [PMID: 15204876 DOI: 10.1080/15459620490424500]
- 24 **Grivna M**, Eid HO, Abu-Zidan FM. Epidemiology of burns in the United Arab Emirates: lessons for prevention. *Burns* 2014; **40**: 500-505 [PMID: 24011735 DOI: 10.1016/j.burns.2013.08.010]
- 25 **Rosberg HE**, Dahlin LB. Epidemiology of hand injuries in a middle-sized city in southern Sweden: a retrospective comparison of 1989 and 1997. *Scand J Plast Reconstr Surg Hand Surg* 2004; **38**: 347-355 [PMID: 15841802 DOI: 10.1080/02844310410022117]
- 26 **Eid HO**, Hefny AF, Abu-Zidan FM. Epidemiology of animal-related injuries in a high-income developing country. *Ulus Travma Acil Cerrahi Derg* 2015; **21**: 134-138 [PMID: 25904275 DOI: 10.5505/tjtes.2015.76508]
- 27 **Abu-Zidan FM**, Hefny AF, Eid HO, Bashir MO, Branicki FJ. Camel-related injuries: prospective study of 212 patients. *World J Surg* 2012; **36**: 2384-2389 [PMID: 22689019 DOI: 10.1007/s00268-012-1673-2]
- 28 **Durusoy R**, Davas A, Kayalar M, Bal E, Aksu F, Ada S. What kinds of hand injuries are more likely to result in amputation? An analysis of 6549 hand injuries. *J Hand Surg Eur Vol* 2011; **36**: 383-391 [PMID: 21406567 DOI: 10.1177/1753193411400520]
- 29 **Panagopoulou P**, Antonopoulos CN, Iakovakis I, Dessypris N, Gkiokas A, Pasparakis D, Michelakos T, Kanavidis P, Soucacos PN, Petridou ET. Traumatic hand amputations among children in Greece: epidemiology and prevention potential. *Inj Prev* 2012; **18**: 309-314 [PMID: 22180619 DOI: 10.1136/injuryprev-2012-040590m.27]
- 30 **Schier JS**, Chan J. Changes in life roles after hand injury. *J Hand Ther* 2007; **20**: 57-68; quiz 69 [PMID: 17254909 DOI: 10.1197/j.jht.2006.10.005]
- 31 **Maghsoudipour M**, Sarfaraz Z. Industrial workers with occupational hand injury from Tehran factories. *Work* 2011; **40**: 211-215 [PMID: 21876275 DOI: 10.3233/WOR-2011-1221]
- 32 **Lombardi DA**, Jin K, Vetter C, Courtney TK, Folkard S, Arlinghaus A, Liang Y, Perry MJ. The impact of shift starting time on sleep duration, sleep quality, and alertness prior to injury in the People's Republic of China. *Chronobiol Int* 2014; **31**: 1201-1208 [PMID: 25216207 DOI: 10.3109/07420528.2014.957303]
- 33 **American College of Surgeons**. Injury Prevention and Control. 2016. Available from: URL: <https://www.facs.org/quality-programs/trauma/ipc>
- 34 **Royal Australasian College of Surgeons**. Appendix to Policy on Trauma (injury). Royal Australasian College of Surgeons, 2004: 7
- 35 **Eid HO**, Abu-Zidan FM. Pedestrian injuries-related deaths: a global evaluation. *World J Surg* 2015; **39**: 776-781 [PMID: 25373685 DOI: 10.1007/s00268-014-2853-z]

P- Reviewer: Bassetto F, Hamasaki T, Kovar FM
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Prospective Study

Risk assessment instruments for screening bone mineral density in a Mediterranean population

Sotirios Christodoulou, Georgios I Drosos, Athanasios Ververidis, Antonios Galanos, George Anastassopoulos, Konstantinos Kazakos

Sotirios Christodoulou, Georgios I Drosos, Athanasios Ververidis, Konstantinos Kazakos, Department of Orthopaedic Surgery, Democritus University of Thrace, University General Hospital of Alexandroupolis, Dragana, 68100 Alexandroupolis, Greece

Antonios Galanos, Laboratory for Research of the Musculoskeletal System, University of Athens, KAT Hospital, Kifissia, 14561 Athens, Greece

George Anastassopoulos, Medical Informatics Laboratory, Medical School, Democritus University of Thrace, Dragana, 68100 Alexandroupolis, Greece

Author contributions: Christodoulou S drafted the manuscript; Drosos GI and Ververidis A participated in study design and edited the manuscript; Galanos A and Anastasopoulos G performed data analysis; Kazakos K provided oversight to manuscript development, recruited patients, and collected data; all authors read and approved the final manuscript.

Institutional review board statement: This study was approved by the Democritus University of Thrace Medical Institutional Review Boards.

Informed consent statement: All study participants provided written consent prior to study enrollment.

Conflict-of-interest statement: The authors have no conflicts of interest to disclose.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Georgios I Drosos, MD, PhD, Associate

Professor of Orthopaedics, Department of Orthopaedic Surgery, Democritus University of Thrace, University General Hospital of Alexandroupolis, St. Niarhos Street 1, Dragana, 68100 Alexandroupolis, Greece. drosos@otenet.gr
Telephone: +30-6944-380694
Fax: +30-25510-30370

Received: March 27, 2016
Peer-review started: March 30, 2016
First decision: May 13, 2016
Revised: June 1, 2016
Accepted: July 14, 2016
Article in press: July 18, 2016
Published online: September 18, 2016

Abstract

AIM

To evaluate the power of six osteoporosis-screening instruments in women in a Mediterranean country.

METHODS

Data concerning several osteoporosis risk factors were prospectively collected from 1000 postmenopausal women aged 42-87 years who underwent dual-energy X-ray absorptiometry (DEXA) screening. Six osteoporosis risk factor screening tools were applied to this sample to evaluate their performance and choose the most appropriate tool for the study population.

RESULTS

The most important screening tool for osteoporosis status was the Simple Calculated Osteoporosis Risk Estimation, which had an area under the curve (AUC) of 0.678, a sensitivity of 72%, and a specificity of 72%, with a cut-off point of 20.75. The most important screening tool for osteoporosis risk was the Osteoporosis Self-assessment Tool, which had an AUC of 0.643, a sensitivity of 77%, and a specificity of 46%.

with a cut-off point of -2.9.

CONCLUSION

Some commonly used clinical risk instruments demonstrate high sensitivity for distinguishing individuals with DEXA-ascertained osteoporosis or reduced bone mineral density.

Key words: Osteoporosis; Bone mineral density; Risk assessment; Dual X-ray absorptiometry; Osteopenia

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Bone mineral density (BMD) measurement using dual-energy X-ray absorptiometry (DEXA) is currently the most widely used method for osteoporosis screening, treatment and patient monitoring. Nevertheless, performing routine BMD measurements of all women is not feasible for most populations, and at present there is no universally accepted policy for population screening in Europe to identify patients with osteoporosis or those at high risk of fracture. Osteoporosis risk factor screening tools have been developed to identify postmenopausal women in need of DEXA screening and possible intervention for osteoporosis.

Christodoulou S, Drosos GI, Ververidis A, Galanos A, Anastasopoulos G, Kazakos K. Risk assessment instruments for screening bone mineral density in a Mediterranean population. *World J Orthop* 2016; 7(9): 577-583 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/577.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.577>

INTRODUCTION

Osteoporosis is the most common bone disease, characterized by low bone mass and microarchitecture deterioration, which increase bone fragility and susceptibility to fracture^[1]. Distal forearm fractures, vertebra fractures and proximal femoral (hip) fractures are typical osteoporotic fractures. However, patients with low bone mineral density (BMD) are at high risk for all types of fractures, irrespective of fracture site^[2].

An estimated 50% of Caucasian women and 20% of Caucasian men older than 50 years will experience a fragility fracture in their lifetime^[3]. This is an important public health issue because many of these fractures are associated with increased mortality, morbidity or permanent disability, as well as high societal and personal costs^[4]. Identification and treatment of patients, particularly women, at risk for osteoporosis is of great importance for the prevention of osteoporotic fractures^[5].

BMD measurement using dual-energy X-ray absorptiometry (DEXA) is currently the most widely used method to diagnose osteoporosis (*i.e.*, provide criteria for fracture risk), to guide treatment decisions and to monitor patient course after receiving or not receiving

treatment^[6]. Nevertheless, routine BMD measurement of all women is not feasible for most populations because of lack of scanners, lack of awareness or lack of widely accepted guidelines. At present, there is no universally accepted policy for population screening in Europe to identify patients with osteoporosis or those at high risk of fracture.

Additionally, the various osteoporosis-screening instruments that exist to help clinicians identify women at increased risk for osteoporosis who should undergo further testing in combination with DEXA screening^[7].

The aim of this survey was to evaluate the power of six osteoporosis-screening instruments^[8-13] in identifying postmenopausal women at risk of developing osteoporosis in a Mediterranean country. More specifically, our aim was to evaluate these clinical risk estimation instruments in distinguishing individuals with DEXA-identified osteoporosis or reduced BMD while sustaining specific levels of sensitivity and specificity for select cut-off values to identify individuals with BMD T-scores beneath a defined DEXA score.

MATERIALS AND METHODS

Patients

This cross-sectional study utilized prospectively collected data from the Bone Density Measurement Unit of the Department of Orthopaedic Surgery at University General Hospital of Alexandroupolis, a tertiary hospital. The study was approved by the Ethics Committee of the hospital, and informed consent was obtained from all participants.

The study included postmenopausal women (> 12 mo since last menstrual period). Women receiving medication for either the prevention or treatment of diagnosed osteoporosis were excluded.

All the study subjects underwent DEXA screening between October 1, 2012 and October 1, 2014. Confirmation of osteoporosis occurred through BMD measurements, which were compared with the results of the other analytical tools used.

Additionally, the following information was obtained from each patient: Age, weight, height, various osteoporosis risk factors (*i.e.*, a history of fragility fractures of the spine or hip that occurred after age 50 years), parental hip fracture, ever or current long-term use of steroids (> 3 mo use), current smoking, small stature (body mass index < 21 kg/m²), medical history of rheumatoid arthritis, other medical causes of bone loss (*i.e.*, hyperthyroidism, hyperparathyroidism, kidney failure, or anorexia), use of long-term therapy with medications known to adversely affect BMD (*i.e.*, heparin or anticonvulsants), use of arms to stand up (as an indicator of physical activity), ever or current hormonal therapy, concomitant medications, and family and personal medical histories. The results from each DEXA screen were obtained and incorporated into the database.

Screening tools

In this study, six screening tools^[8-13] were applied to

Table 1 Criteria for clinical decision rules and osteoporotic risk factors

SCORE	Age, body weight (kg), race, hormone therapy use, fracture history, history of rheumatoid arthritis
ORAI	Age, body weight (kg), hormone therapy use
OST	Age, body weight (kg)
BW	Body weight (kg)
OSIRIS	Age, body weight (kg), hormone therapy use, fracture history
ABONE	Age, body size, lack of estrogen

SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; OST: Osteoporosis self-assessment tool; BW: Body weight; OSIRIS: Osteoporosis index of risk; ABONE: Age, body size, no estrogen.

evaluate a sample of Greek postmenopausal women. The performance of the tools was compared to select the most suitable instrument for this population.

The simple calculated osteoporosis risk estimation (SCORE) was formulated by Lydick *et al.*^[8] and accounts for 6 risk factors (Table 1). The SCORE possesses a sensitivity ranging from 0.80 to 1.00 and a specificity ranging from 0.40 to 0.50.

The osteoporosis risk assessment instrument (ORAI) was formulated by Cadarette *et al.*^[9] and accounts for 3 risk factors (Table 1). The ORAI has a sensitivity of 0.90 and a specificity of 0.45.

The osteoporosis self-assessment tool (OST) was formulated by Geusens *et al.*^[10] for evaluation of Asian and Caucasian women. It utilizes 2 factors (Table 1) and shows a sensitivity of 0.88 and a specificity of 0.52.

The body weight criterion (BW) was formulated by Michaëlsson *et al.*^[11] and accounts for only one factor (Table 1). It has a sensitivity of 0.94 and a specificity of 0.36.

The osteoporosis index of risk (OSIRIS) was formulated by Sedrine *et al.*^[12] using four factors (Table 1). It has a sensitivity of 0.79 and a specificity of 0.51.

Weinstein and Ullery^[13] formulated the Age, Body size, No Estrogen tool (ABONE) (Table 1), which has a high specificity of 0.84 but a low sensitivity of 0.56.

Statistical analysis

Data are expressed as the mean \pm SD or the median (IQR) for quantitative data and as percentages for qualitative data. The Kolmogorov-Smirnov test was utilized for normality analyses of the parameters. A receiver operating curve (ROC) analysis was conducted to determine the diagnostic abilities and obtain the cut-off levels of the various osteoporosis-screening tools in classifying patients as osteoporotic or at high osteoporotic risk. This was accomplished according to T-score classification by calculating the areas under the curve (AUC) and their standard errors and 95% CIs. To evaluate the internal credibility of the indices, sensitivity was delineated as the proportion of the population with reduced BMD who were correctly categorized by the risk index (true positive fraction), and specificity was delineated as the proportion

of the population with normal BMD who were correctly categorized by the risk index (true negative fraction).

We also measured the positive predictive value (PPV) and negative predictive value (NPV) of each instrument to measure their external credibility. The PPV and NPV corresponded to the average numbers of women who were deemed as positive or negative (as compared by the four instruments), respectively, who truly had or did not have BMD values beneath the T-score cut-off.

The ROC curves were used to provide a graphical interpretation of the general quality of each test by plotting sensitivity against (1-specificity) for all thresholds, while the AUC values were used to indicate test quality. Multiple logistic regression analysis using the enter method was performed with the dependent variables (T-score \leq -2.5 vs T-score $>$ -2.5) and (T-score \leq -2 vs T-score $>$ -2) and the osteoporosis-screening indices as the independent variables. All the tests were two-sided, and statistical significance was set at $P < 0.05$. All analyses were carried out using SPSS ver 17.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Ill., United States).

RESULTS

One thousand women with a mean age of 63.41 years (minimum 42 years and maximum 87 years) were included in this study. The mean age at menarche was 13.2 years (minimum 8 years and maximum 18 years), and the mean weight and height were 73.52 kg (minimum 40 kg and maximum 120 kg) and 1.59 m (minimum 1.42 m and maximum 1.80 m). The mean number of pregnancies was 2.3 (0-12 pregnancies), the mean alcohol consumption was 0.37 drinks weekly (0-7 drinks), and the mean coffee consumption was 1.60 cups daily (0-6 cups). Additionally, 12.1% of the population were smokers, 64.5% had previously experienced a graduated fracture, 20% regularly exercised, 20% had kyphosis, 2.7% had rheumatoid arthritis, 3.8% had received hormone therapy, and 3.2% had received cortisone.

The following indicator values were obtained: BW: 73.52 \pm 11.32, OST: -2.02 \pm 2.94, ORAI: 10.05 \pm 5.02, SCORE: 20.54 \pm 3.70, OSIRIS: 0.68 \pm 3.14 and ABONE: 1.54 \pm 0.66. The AUC ratios and the sensitivities and specificities of the instruments for identifying high osteoporotic risk and osteoporosis were assessed using cut-off points from the literature. The tool with the highest AUC value was the ABONE (AUC: 0.628), followed by the ORAI (AUC: 0.608).

The highest levels of sensitivity and accuracy in identifying patients at high risk of osteoporosis were obtained by the ORAI (72%) and the ABONE (65%). The highest levels of sensitivity and accuracy in diagnosing osteoporosis were obtained by the OSIRIS (63%) and the BW (67%). The sensitivity for the OSIRIS was 0.631, and the specificity was 0.570. The sensitivity for the BW was 0.40, and the specificity was 0.667. These values are listed in Table 2.

Table 2 Receiver operating curve analysis using international guidelines

	AUC	95%CI		Sensitivity	Specificity	P-value
SCORE ¹	---	---	---	---	---	---
ORAI ¹	0.608	0.57	0.65	0.716	0.498	< 0.0005
ABONE ¹	0.628	0.59	0.67	0.650	0.610	< 0.0005
BW ²	0.535	0.49	0.58	0.400	0.667	0.109
OST ²	0.586	0.54	0.63	0.515	0.312	< 0.0005
OSIRIS ²	0.600	0.56	0.64	0.631	0.570	< 0.0005

¹Osteoporosis risk T-score < -2; ²Osteoporosis status T-score < -2.5.
AUC: Area under the curve; SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; ABONE: Age, body size, no estrogen; BW: Body weight; OST: Osteoporosis self-assessment tool; OSIRIS: Osteoporosis index of risk.

The AUC, sensitivity, and specificity values and the cut-off points for the indicators of osteoporosis risk are presented in Table 3. The clinical tool with the highest AUC value was the OST (AUC: 0.643), followed by the ORAI (AUC: 0.640) and the ABONE (AUC: 0.631). The highest sensitivity in identifying patients at high risk for osteoporosis was obtained with the OST (77%), followed by the ORAI (72%) and the ABONE (65%). The highest accuracy for identifying individuals at high osteoporotic risk was obtained by the BW (61%), followed by the SCORE (60%). The sensitivity of the BW was 51%, and its specificity was 61%. The sensitivity and specificity for the SCORE were 61% and 60%, respectively.

The AUC, sensitivity, and specificity values and the cut-off points for the indicators of osteoporotic condition are shown in Table 4. The clinical tool with the highest AUC value was the SCORE (AUC: 0.678), followed by the OST (AUC: 0.644) and the OSIRIS (AUC: 0.641). The highest sensitivity in diagnosing osteoporosis was obtained with the OST (80%), followed by the OSIRIS (76%) and the SCORE (65%). The highest accuracy for assessing osteoporotic status was obtained with the ORAI (60%) and the SCORE (60%).

The sensitivity for the OST was 80%, and its specificity was 43%. The sensitivity and specificity for the OSIRIS were 76% and 44%, respectively. For the SCORE, the sensitivity and specificity were 72% and 60%, respectively. For the ORAI, the specificity and sensitivity were 65% and 60%, respectively.

The results from the multiple logistic regression analysis for the variable high osteoporotic risk are presented in Table 5. For this analysis, we introduced each of the variables into a multiple linear regression model (known as the enter method) to identify the independent effects of each instrument on the variable high osteoporotic risk. We found that the OST ($P = 0.012$), ABONE ($P = 0.051$) and SCORE ($P = 0.081$) each had a statistically significant effect on this variable.

The results from the multiple logistic regression analysis for the variable osteoporosis are presented in Table 6. Similar to the above, we used the enter method to identify the independent effects of each instrument on the variable osteoporosis. Only the SCORE ($P < 0.0005$)

had a statistically significant effect on this variable.

DISCUSSION

In this survey, we assessed the performance of six osteoporosis pre-screening models in evaluating a sample of Greek postmenopausal women and selected the most suitable instrument for that population. Our results exhibited that, assuming a -2.5 cut-off for T-score in three areas of concern, the OST and the OSIRIS had equal predictive precision (AUCs between 0.586 and 0.6). Additionally, assuming a -2 cut-off for T-score in three areas of concern, the ORAI and the ABONE had equal predictive precision (AUCs between 0.608 and 0.628). The least suitable and least useful model based on AUC was the BW, which had only 40% sensitivity. The ABONE and the ORAI were more suitable models, each with an AUC of approximately 0.628.

When considering the AUCs, sensitivities, specificities and cut-off points for the indicators of patients at high-risk of osteoporosis, the clinical tool with the highest AUC value was the OST (AUC: 0.643), followed by the ORAI (AUC: 0.640) and the ABONE (AUC: 0.631).

With regard to the AUCs, sensitivities, specificities and cut-off points for osteoporosis, the clinical tool with the highest AUC value was the SCORE (AUC: 0.678), followed by the OST (AUC: 0.644) and the OSIRIS (AUC: 0.641).

Combining the above criteria, in the Greek postmenopausal population, the most important screening tool for osteoporosis status is the SCORE, and for osteoporotic risk, it is the OST. In our study, the SCORE had an AUC of 0.678, a sensitivity of 72%, and a specificity of 72%, with a cut-off point of 20.75, for osteoporosis status. Additionally, the screening tool most important for osteoporosis risk was the OST. The OST had an AUC of 0.643, a sensitivity of 77%, and a specificity of 46%, with a cut-off point of -2.9.

These results must be interpreted with caution, as they are based on a sample of only 1000 patients and may not represent the entire Greek population.

As clinical decision tools, instruments used to predict osteoporosis risk and to identify osteoporosis should be straightforward and convenient to apply in clinical practice in addition to being accurate. Nevertheless, when applying such instruments to different countries or populations, their reported utility has varied amongst different studies. It has been found that they perform well in classifying the risk of osteoporosis and that applying them is more prudent than the use of the BMD^[14]. However, clinical decision-making tools were found to have limited utility for predicting osteoporosis in patients with rheumatoid arthritis^[15]. Wallace *et al*^[16] reported sensitivities of 83% for the SCORE and 65% for the ORAI. Martínez-Aguilà *et al*^[17] found sensitivities of 64% for the ORAI and 83% for the BW in Spanish women, while Cass *et al*^[18] reported sensitivities of 66% for the SCORE and 68% for the ORAI in a group of Caucasian (non-Hispanic and Hispanic) and African-

Table 3 Receiver operating curve analysis using Greek population values for osteoporosis risk

	Area	95%CI		Cut-off	Sensitivity	Specificity	PPV	NPV	P-value
SCORE ¹	0.613	0.576	0.650	20.75 >	61%	60%	46%	73%	< 0.0005
ORAI ¹	0.640	0.603	0.676	9.5 >	72%	52%	46%	76%	< 0.0005
ABONE ¹	0.631	0.595	0.668	10.5 >	62%	62%	48%	74%	< 0.0005
OST ¹	0.643	0.607	0.678	1.5 >	65%	41%	32%	85%	< 0.0005
BW ¹	0.592	0.555	0.630	-2.9 >	77%	46%	45%	78%	< 0.0005
OSIRIS ¹	0.609	0.572	0.645	70.5 <	51%	61%	42%	68%	< 0.0005
				0.5 <	59%	59%	44%	71%	< 0.0005

¹High risk for osteoporosis: T-score \leq -2. SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; ABONE: Age, body size, no estrogen; OST: Osteoporosis self-assessment tool; BW: Body weight; OSIRIS: Osteoporosis index of risk; PPV: Positive predictive value; NPV: Negative predictive value.

Table 4 Receiver operating curve analysis using Greek population values for osteoporosis status

	Area	95%CI		Cut-off	Sensitivity	Specificity	PPV	NPV	P-value
SCORE ¹	0.678	0.640	0.717	20.75 >	72%	60%	36%	87%	< 0.0005
ORAI ¹	0.632	0.591	0.673	10.5 >	65%	60%	33%	85%	< 0.0005
ABONE ¹	0.618	0.576	0.659	1.5 >	66%	60%	48%	75%	< 0.0005
OST ¹	0.644	0.604	0.684	-2.9 >	80%	43%	30%	87%	< 0.0005
BW ¹	0.591	0.549	0.633	75.5 <	69%	41%	26%	81%	< 0.0005
OSIRIS ¹	0.641	0.601	0.681	0.5 <	63%	57%	31%	83%	< 0.0005
				1.5 <	76%	44%	30%	86%	< 0.0005

¹Osteoporosis status: T-score \leq -2.5. SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; ABONE: Age, body size, no estrogen; OST: Osteoporosis self-assessment tool; BW: Body weight; OSIRIS: Osteoporosis index of risk; PPV: Positive predictive value; NPV: Negative predictive value.

Table 5 Multiple logistic regression model (T-score \leq -2)

	Reference category	Odds ratio	95%CI		P-value
SCORE	20.75 <	1.36	0.96	1.91	0.081
ORAI	10.5 <	1.30	0.8	2.09	0.287
ABONE	1.5 <	1.64	1.00	2.70	0.051
OST	-2.9 <	1.81	1.14	2.88	0.012
BW	70.5 >	1.05	0.75	1.47	0.772
OSIRIS	0.5 >	0.78	0.52	1.16	0.214

SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; ABONE: Age, body size, no estrogen; OST: Osteoporosis self-assessment tool; BW: Body weight; OSIRIS: Osteoporosis index of risk.

Table 6 Multiple logistic regression model (T-score \leq -2.5)

	Reference category	Odds ratio	95%CI		P-value
SCORE	20.75 <	2.87	1.92	4.29	< 0.0005
ORAI	10.5 <	1.42	0.81	2.48	0.215
ABONE	1.5 <	0.95	0.53	1.70	0.865
OST	-2.9 <	1.55	0.90	2.65	0.115
BW	70.5 >	1.10	0.76	1.60	0.600
OSIRIS	0.5 >	0.88	0.56	1.39	0.586

SCORE: Simple calculated osteoporosis risk estimation; ORAI: Osteoporosis risk assessment instrument; ABONE: Age, body size, no estrogen; OST: Osteoporosis self-assessment tool; BW: Body weight; OSIRIS: Osteoporosis index of risk.

American women. A recent systematic review concerning the performance of the OST found that this tool may be of clinical value in ruling out low BMD^[19], while another systematic review focused on accuracy that compared the OST to the SCORE and the ORAI produced similar results^[20].

When comparing the different studies that have focused on the performance of these instruments, two notable points arise. The first concerns the threshold for defining osteoporosis; in particular, some tools (such as the ORAI and the ABONE) were developed using as a T-score \leq -2.0 as a threshold, while other tools (such as the BW and the OSIRIS) use a T-score \leq -2.5 as a threshold. A lower threshold provides more robust and defined segmentation for prophylactic strategies and helps in assigning screening intervals^[21]. The second point concerns the skeletal site that is tested for BMD, as

different BMD values have been measured at different anatomic sites within the same patient. It has been suggested that a value beneath the determined threshold at any site (lumbar spine or hip) is sufficient^[22].

Study limitation

The main limitation of our study is the small population evaluated. The information we gathered specifically pertains to women who were seen at university hospital in Alexandroupolis, Eastern-Macedonia and Thrace. However, as a notable strength, our study is the most inclusive evaluation of clinical risk assessment instruments for distinguishing Greek postmenopausal women with osteoporosis or reduced BMD.

In conclusion, our study identified clinical risk instruments that showed high sensitivity for identifying individuals with DEXA-determined osteoporosis or low BMD.

We believe that further studies from other centers in our region concerning the effectiveness of these instruments are required.

COMMENTS

Background

Osteoporosis is the most common bone disease, characterized by low bone mass and microarchitecture deterioration, which increase bone fragility and susceptibility to fracture. Dual-energy X-ray absorptiometry (DEXA) is currently the most widely used method to diagnose low bone mass, but routine bone mineral density (BMD) measurement of all women is not feasible for most populations, and universally accepted guidelines do not exist.

Research frontiers

Clinical risk assessment instruments for distinguishing individuals with osteoporosis or reduced BMD have been formulated to identify postmenopausal women who should undergo DEXA measurement for osteoporosis. Nevertheless, applying these instruments in different countries or populations has shown varied utility amongst previous studies.

Innovations and breakthroughs

In the current study, the authors utilized six osteoporosis pre-screening instruments on a sample of Greek postmenopausal women to standardize their interpretation and select the most suitable instrument for that population. With consideration of the factors identified in other instrument validations, we showed that using -2.5 as a cut-off T-score in three areas of interest for the studied osteoporosis self-assessment tools and osteoporosis index of risk produced the highest precision [area under the curve (AUC) between 0.586 and 0.6]. At the same time, using -2 as a cut-off T-score in three areas of interest in the studied osteoporosis risk assessment instruments while accounting for age, body size, and lack of estrogen produced the highest precision (AUC between 0.608 and 0.628).

Applications

The purpose of this study was to measure the performance of a panel of clinical risk instruments in identifying individuals with DEXA-determined osteoporosis or reduced BMD in a Mediterranean population. Specifically, the authors measured the sensitivity and specificity associated with different cut-off values to identify individuals with BMD T-scores beneath a nominal DEXA threshold.

Terminology

Osteoporosis is a skeletal disease characterized by low bone mass and microarchitecture deterioration, which increase bone fragility and susceptibility to fracture. BMD measurement using DEXA is currently the most widely used method to diagnose osteoporosis (*i.e.*, provide criteria for fracture risk), guide its treatment and monitor patient course after receiving or not receiving treatment. Osteoporosis risk factor clinical risk assessment instruments for distinguishing individuals with osteoporosis or reduced BMD were formulated to identify postmenopausal women who should undergo DEXA measurement for osteoporosis.

Peer-review

This is an interesting paper with regards to the argument of screening tools for osteoporosis and identification of the patients that need to have DEXA measurement. Furthermore, it adds information missing in this area of the Mediterranean Sea.

REFERENCES

- 1 Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002; **359**: 1761-1767 [PMID: 12049882 DOI: 10.1016/S0140-6736(02)08657-9]
- 2 Kanis JA, Johnell O, De Laet C, Johansson H, Oden A, Delmas P, Eisman J, Fujiwara S, Garnero P, Kroger H, McCloskey EV, Mellstrom D, Melton LJ, Pols H, Reeve J, Silman A, Tenenhouse A. A meta-analysis of previous fracture and subsequent fracture risk. *Bone* 2004; **35**: 375-382 [PMID: 15268886 DOI: 10.1016/j.bone.2004.03.024]
- 3 Melton III L, Cooper C. Magnitude and impact of osteoporosis and fractures. In: Marcus R, Feldman D, Kelsey J. Osteoporosis. 2nd ed. San Diego: Academic Press, 2001: 557-567
- 4 Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int* 2006; **17**: 1726-1733 [PMID: 16983459 DOI: 10.1007/s00198-006-0172-4]
- 5 Johnell O. The socioeconomic burden of fractures: today and in the 21st century. *Am J Med* 1997; **103**: 20S-25S; discussion 25S-26S [PMID: 9302894 DOI: 10.1016/S0002-9343(97)90023-1]
- 6 Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int* 2013; **24**: 23-57 [PMID: 23079689 DOI: 10.1007/s00198-012-2074-y]
- 7 Cadarette SM, Jaglal SB, Kreiger N, McIsaac WJ, Darlington GA, Tu JV. Development and validation of the Osteoporosis Risk Assessment Instrument to facilitate selection of women for bone densitometry. *CMAJ* 2000; **162**: 1289-1294 [PMID: 10813010 DOI: 10.1007/s00198-008-0560-z]
- 8 Lydick E, Cook K, Turpin J, Melton M, Stine R, Byrnes C. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. *Am J Manag Care* 1998; **4**: 37-48 [PMID: 10179905]
- 9 Cadarette SM, Jaglal SB, Murray TM, McIsaac WJ, Joseph L, Brown JP. Evaluation of decision rules for referring women for bone densitometry by dual-energy x-ray absorptiometry. *JAMA* 2001; **286**: 57-63 [PMID: 11434827 DOI: 10.1001/jama.286.1.57]
- 10 Geusens P, Hochberg MC, van der Voort DJ, Pols H, van der Klift M, Siris E, Melton ME, Turpin J, Byrnes C, Ross P. Performance of risk indices for identifying low bone density in postmenopausal women. *Mayo Clin Proc* 2002; **77**: 629-637 [PMID: 12108600 DOI: 10.4065/77.7.629]
- 11 Michaëlsson K, Bergström R, Mallmin H, Holmberg L, Wolk A, Ljunghall S. Screening for osteopenia and osteoporosis: selection by body composition. *Osteoporos Int* 1996; **6**: 120-126 [PMID: 8704349 DOI: 10.1007/BF01623934]
- 12 Sedrine WB, Chevallier T, Zegels B, Kvasz A, Micheletti MC, Gelas B, Reginster JY. Development and assessment of the Osteoporosis Index of Risk (OSIRIS) to facilitate selection of women for bone densitometry. *Gynecol Endocrinol* 2002; **16**: 245-250 [PMID: 12192897 DOI: 10.1080/gye.16.3.245.250]
- 13 Weinstein L, Ullery B. Identification of at-risk women for osteoporosis screening. *Am J Obstet Gynecol* 2000; **183**: 547-549 [PMID: 10992172 DOI: 10.1067/mob.2000.106594]
- 14 Koh LK, Sedrine WB, Torralba TP, Kung A, Fujiwara S, Chan SP, Huang QR, Rajatanavin R, Tsai KS, Park HM, Reginster JY. A simple tool to identify asian women at increased risk of osteoporosis. *Osteoporos Int* 2001; **12**: 699-705 [PMID: 11580084 DOI: 10.1007/s001980170070]
- 15 Brand C, Lowe A, Hall S. The utility of clinical decision tools for diagnosing osteoporosis in postmenopausal women with rheumatoid arthritis. *BMC Musculoskelet Disord* 2008; **9**: 13 [PMID: 18230132 DOI: 10.1186/1471-2474-9-13]
- 16 Wallace LS, Ballard JE, Holiday D, Turner LW, Keenum AJ, Pearman CM. Evaluation of decision rules for identifying low bone density in postmenopausal African-American women. *J Natl Med Assoc* 2004; **96**: 290-296 [PMID: 15040510]
- 17 Martínez-Aguilà D, Gómez-Vaquero C, Rozadilla A, Romera M, Narváez J, Nolla JM. Decision rules for selecting women for bone mineral density testing: application in postmenopausal women referred to a bone densitometry unit. *J Rheumatol* 2007; **34**: 1307-1312 [PMID: 17552058]
- 18 Cass AR, Shepherd AJ, Carlson CA. Osteoporosis risk assessment and ethnicity: validation and comparison of 2 clinical risk stratification instruments. *J Gen Intern Med* 2006; **21**: 630-635 [PMID: 16808748 DOI: 10.1111/j.1525-1497.2006.00459.x]
- 19 Rud B, Hilden J, Hyldstrup L, Hróbjartsson A. Performance of the Osteoporosis Self-Assessment Tool in ruling out low bone mineral density in postmenopausal women: a systematic review.

- Osteoporos Int* 2007; **18**: 1177-1187 [PMID: 17361324 DOI: 10.1007/s00198-006-0319-3]
- 20 **Rud B**, Hilden J, Hyldstrup L, Hróbjartsson A. The Osteoporosis Self-Assessment Tool versus alternative tests for selecting postmenopausal women for bone mineral density assessment: a comparative systematic review of accuracy. *Osteoporos Int* 2009; **20**: 599-607 [PMID: 18716823 DOI: 10.1007/s00198-008-0713-0]
- 21 **Kanis JA**, Melton LJ, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. *J Bone Miner Res* 1994; **9**: 1137-1141 [PMID: 7976495 DOI: 10.1002/jbmr.5650090802]
- 22 **Looker AC**, Borrud LG, Dawson-Hughes B, Shepherd JA, Wright NC. Osteoporosis or low bone mass at the femur neck or lumbar spine in older adults: United States, 2005-2008. *NCHS Data Brief* 2012; (**93**): 1-8 [PMID: 22617299]

P- Reviewer: Cartmell S, Drampalos E

S- Editor: Gong XM **L- Editor:** A **E- Editor:** Li D



Total knee arthroplasty for treatment of post-traumatic arthritis: Systematic review

Hesham Saleh, Stephen Yu, Jonathan Vigdorichik, Ran Schwarzkopf

Hesham Saleh, Stephen Yu, Jonathan Vigdorichik, Ran Schwarzkopf, Division of Adult Reconstruction, Department of Orthopaedic Surgery, New York University Langone Medical Center, Hospital for Joint Diseases, New York, NY 10003, United States

Author contributions: Saleh H drafted the initial manuscript; Saleh H and Yu S performed the research; Saleh H, Yu S, Vigdorichik J and Schwarzkopf R contributed equally to the work; Vigdorichik J and Schwarzkopf R conceptualized and designed the review; all authors reviewed and approved the final manuscript as submitted.

Conflict-of-interest statement: None of the authors have relevant disclosures to make in relation to the submitted study. Schwarzkopf R received research funding, speaker fees, consulting fees, or royalties from Smith and Nephew, Intelijoint. None of the authors own company stock or options. None of the authors own any patents. Schwarzkopf R and Vigdorichik J are on the editorial board Journal of Arthroplasty, Arthroplasty today. None of the authors are a board member of any societies.

Data sharing statement: All technical data is available from the corresponding author at schwarzk@gmail.com. Consent was not obtained for data sharing but the presented data is anonymized and the risk of identification is low.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Ran Schwarzkopf, MD, MSc, Division of Adult Reconstruction, Department of Orthopaedic Surgery, New York University Langone Medical Center, Hospital for Joint Diseases, 301 E 17th Street, New York, NY 10003, United States. ran.schwarzkopf@nyumc.org
Telephone: +1-212-5137711

Received: March 27, 2016
Peer-review started: March 30, 2016
First decision: May 13, 2016
Revised: May 28, 2016
Accepted: June 27, 2016
Article in press: June 29, 2016
Published online: September 18, 2016

Abstract

AIM

To review and report functional outcomes, complications, and survivorship associated with total knee arthroplasty (TKA) in the treatment of post-traumatic arthritis (PTA).

METHODS

We conducted a systematic review according to the PRISMA guidelines. We searched PubMed, Cochrane Library, and SCOPUS in December 2015 for English-language clinical research studies, both prospective and retrospective, examining the use of TKA for the treatment of PTA. All relevant articles were accessed in full. The manual search included references of retrieved articles. We extracted data on patients' demographics and clinical outcomes, including preoperative diagnosis and pre- and post-operative functional scores. We summarized the data and reported the results in tables and text.

RESULTS

Sixteen studies, four prospective and ten retrospective, examined patients who underwent TKA for PTA due to fractures of the proximal tibia, patella, and/or distal femur. Eleven studies utilized the Knee Society Scores criteria to assess functional outcomes. All studies utilizing these criteria reported an improvement in functional and knee scores of patients following TKA. Further, studies reported an increased range of motion (ROM) and reduction of pain following surgery. The most commonly reported complications with TKA included infection,

stiffness, wound complications, intraoperative rupture of tendons, and osteolysis/polyethylene wear. The overwhelming majority of these complications occurred within the first two years following surgery. Six studies examined the survivorship of TKA with subsequent revision for any reason as an endpoint. Compared to patients with osteoarthritis, patients with PTA required more revisions, the majority for polyethylene wear.

CONCLUSION

Although associated with higher complication rates, TKA is an effective treatment for PTA, as it improves ROM, pain and functional outcomes.

Key words: Total knee arthroplasty; Post-traumatic arthritis; Tibial plateau fracture; Distal femur fracture; Patella fracture

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: There is a paucity in the literature regarding the effectiveness of total knee arthroplasty (TKA) for the treatment of post-traumatic arthritis (PTA). The goal of this systematic review is to summarize the functional outcomes, complications, and survivorship of TKA performed for the treatment of PTA. Majority of studies reported improvements in functional outcomes, increased range of motion, and decreased pain following TKA. There is a significant complication rate, including infection, stiffness, and wound complications. Revisions were performed most commonly for polyethylene wear. Although associated with higher complication rates, TKA is an effective treatment for PTA, as it improves range of motion, pain and functional outcomes.

Saleh H, Yu S, Vighorchik J, Schwarzkopf R. Total knee arthroplasty for treatment of post-traumatic arthritis: Systematic review. *World J Orthop* 2016; 7(9): 584-591 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/584.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.584>

INTRODUCTION

Post-traumatic arthritis (PTA) refers to structural damage following an injury to an articulating joint^[1]. It commonly affects younger, more active individuals as they are more likely to participate in such activities that may cause injury (*i.e.*, sports, blunt trauma, motor vehicle accidents, *etc.*)^[1]. Although any joint in the body may be involved, PTA is often more notable in weight-bearing joints^[1]. It is estimated that 12% of all symptomatic osteoarthritis (OA) of the hip, knee, and ankle are due to PTA^[2]. With a varied prevalence of 21%-44% reported in the literature, PTA of the knee occurs following intra- or extra-articular fractures of the proximal tibia, patella, and distal femur^[3-5]. A combination of factors most likely contributes to the development of PTA following injury

to the knee. First, mechanical imbalance may be due to ligamentous laxity, meniscal tears and malalignment^[1]. Second, the release of pro-inflammatory cytokines into local tissue leads to imperfect remodeling of the cartilage. Lastly, non-unions and malunions following fractures may lead to PTA^[4].

The treatment of PTA can be divided into non-operative and operative management. Activity modification, anti-inflammatory medications, ambulatory assist devices, and physical therapy are the mainstay of non-operative treatment^[1]. After these are exhausted, surgical options range from arthroscopic debridement to arthrodesis^[6]. Total knee arthroplasty (TKA) is an option for the treatment of end-stage PTA^[7].

There is a paucity in the literature regarding TKA for the treatment of PTA. Compared to TKA for patients with primary OA, TKA performed for PTA is often more technically challenging due to previous surgeries and scarring, uses more hospital resources, and incurs a higher cost^[8]. There are conflicting reports in the literature regarding the short and long term outcomes of these surgeries, as well as associated perioperative complications^[8-10]. The goal of this systematic review is to summarize the functional outcomes, complications, and survivorship of TKA performed for the treatment of PTA.

MATERIALS AND METHODS

This systematic review was conducted according to the PRISMA guidelines. A comprehensive search of PubMed, Cochrane Library, and SCOPUS was performed for prospective and retrospective studies examining the use of TKA for the treatment of PTA. The initial search utilized the following key terms: Knee arthroplasty, TKA and traumatic arthritis. English-language studies that examined the short and/or long-term outcomes of TKA performed for traumatic arthritis were included. References from retrieved studies were further reviewed to identify additional articles of interest.

First, inclusion and exclusion criteria were applied to study titles and abstracts independently by two reviewers (Saleh H, Yu S) to identify potentially eligible studies; disagreements were settled and final selections made by a third reviewer (Schwarzkopf R). Studies discussing TKA and traumatic arthritis were included. Studies which focused on unicompartamental knee arthroplasty, osteotomy, and/or patients with primary OA were excluded. Those studies considered potentially eligible were retrieved in full for review. Again, two reviewers independently applied inclusion and exclusion criteria. Studies examining fractures of the proximal tibia, patella, and/or distal femur were included. All study methods, including case-control, cohort, randomized-controlled studies- prospective or retrospective- were included. Case reports, case series, and biomechanics studies were excluded (Figure 1). Included studies were systematically reviewed for methodology (*i.e.*, year of publication, sample size, study type, inclusion/exclusion criteria),

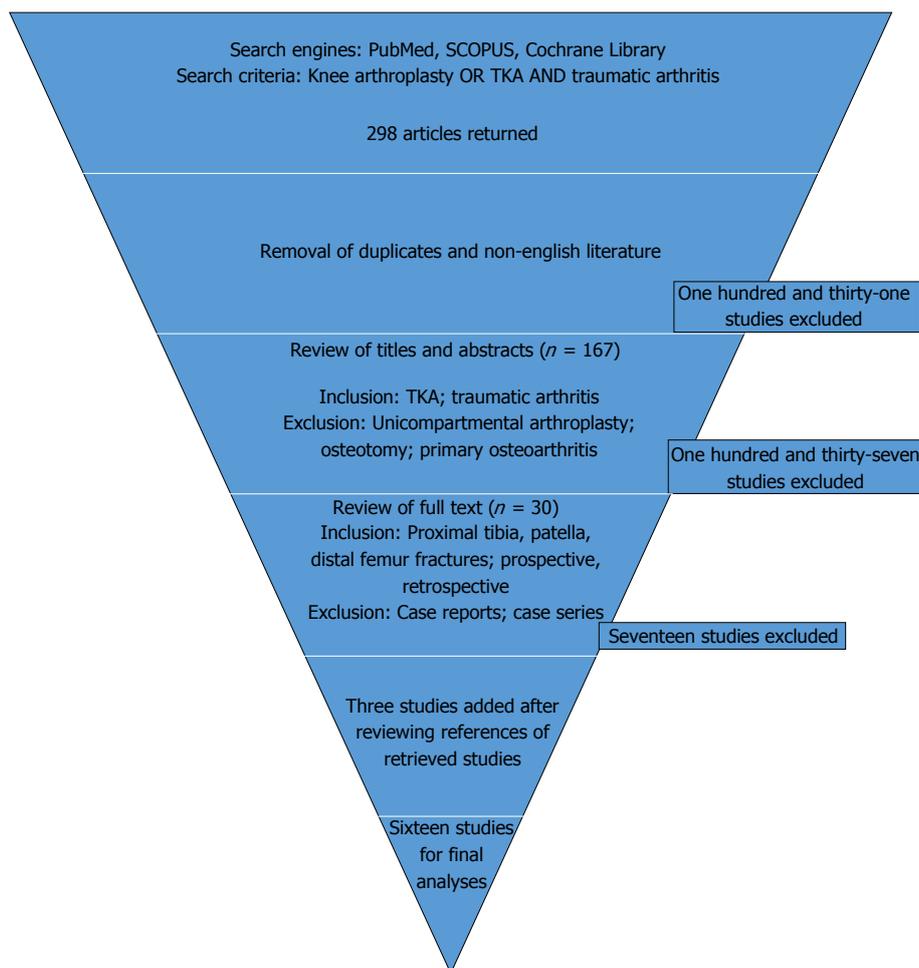


Figure 1 Flowchart summarizing the results of the literature search. TKA: Total knee arthroplasty.

demographics (*i.e.*, age, gender), and clinical outcomes (*i.e.*, follow-up period, preoperative diagnosis, implant selection criteria, pain, functional outcomes).

The main clinical outcomes studied regarding TKA following PTA included patient reported function, knee range of motion, and post-operative pain. Different studies utilized various criteria to assess these outcomes. Hospital for Special Surgery (HSS) Scores, International Knee Scores (IKS), Knee Osteoarthritis Outcomes Scores (KOOS), Oxford Knee Scores, and Knee Society Scores (KSS) were utilized by various studies to analyze the functional outcomes and pain following TKA. KSS was the most commonly utilized, however. The KSS is a 200-point scoring system which ascribes a maximum of 100 points each for function score (ability to walk, climb stairs, and need for assistive devices) and knee score (pain, range of motion, alignment, stability).

All studies examined complications following TKA for the treatment of PTA. The rate of complications was noted, as well as the specific complications observed. Six studies assessed the survivorship of TKA, with the endpoint defined as any subsequent surgery on the same knee. Studies followed patients for different averages of length of time, ranging from 3 to 15 years.

RESULTS

Demographics

Sixteen articles met the inclusion criteria. Ten studies were retrospective, four were prospective (two with the same study cohort), and two were prospective matched cohorts. All studies examined patients with PTA due to fractures of the proximal tibia, patella, and/or distal femur, including nonunions or malunions in three studies. Four studies compared patients with TKA to those with primary OA. The average length of follow-up ranged from 3 to 15 years (Table 1).

Clinical outcomes

Fifteen studies assessed the functional outcomes of TKA for PTA, using different scoring systems such as HSS, IKS, KOOS and KSS. All eleven studies utilizing the KSS criterion showed trends towards or significant improvement between pre- and post- operative function scores (Figure 2). Lizaur-Utrilla *et al.*^[11] reported no difference in the post-operative functional scores of patients with PTA vs primary OA. Lunebourg *et al.*^[8], utilizing the KOOS criteria, reported significantly lower post-operative scores for patients with PTA, compared to primary OA,

Table 1 Demographic information of the studies included in this systematic review

Ref.	Type of study	Total patients	Males (%)	Mean age	Fracture types	Mean follow-up time	Outcome criteria scoring
Abdel <i>et al</i> ^[14]	Prospective	62	36	63	Tibia	15	KSS
Bala <i>et al</i> ^[9]	Retrospective	PTA: 3509 Cont: 257, 611	PTA: 43 Cont: 35	N/A	Tibia/femur	N/A	CCI; Elixhauser
Benazzo <i>et al</i> ^[24]	Prospective	43	47	64	Tibia/femur/patella	6	KSS
Civinini <i>et al</i> ^[25]	Retrospective	25	36	57	Tibia	8	KSS
Deschamps <i>et al</i> ^[23]	Retrospective	78	42	63	Tibia/femur (includes malunions)	4	SOO
Lizaur-Utrilla <i>et al</i> ^[11]	Prospective matched cohort	PTA: 29 Cont: 58	35	PTA: 57.3 Cont: 59.2	Tibia	7	KSS, SF-12, WOMAC
Lonner <i>et al</i> ^[17]	Prospective	30	50	60	Tibia/femur	4	KSS
Lunebourg <i>et al</i> ^[8]	Retrospective	PTA: 33 Cont: 407	PTA: 55 Cont: 32	PTA: 69 Cont: 72	Tibia/femur	11	KSS, KOOS
Massin <i>et al</i> ^[13]	Retrospective	40	10	59	Tibia/femur	5	IKS
Papadopoulos <i>et al</i> ^[22]	Retrospective	47	21	65	Femur (includes malunions)	6	KSS
Parratte <i>et al</i> ^[19]	Retrospective	74	46	63	Tibia/femur/patella (includes malunion)	4	KSS
Saleh <i>et al</i> ^[6]	Retrospective	15	27	56	Tibia	6	HSS, SF-36
Scott <i>et al</i> ^[16]	Prospective matched cohort	PTA: 31 Cont: 93	26	66	Tibia	7	Oxford knee, SF-12
Shearer <i>et al</i> ^[10]	Retrospective	47	62	48	Tibia/femur	4	KSS
Weiss <i>et al</i> ^[12]	Prospective	62	36	63	Tibia	5	KSS
Wu <i>et al</i> ^[26]	Retrospective	15	80	58	Tibia/femur	3	KSS

PTA: Post traumatic arthritis; Cont: Control; OCS: Outcome criteria scoring; IKS: International Knee Scores; KOOS: Knee Osteoarthritis Outcomes Scores; HSS: Hospital for Special Surgery; KSS: Knee Society Scores.

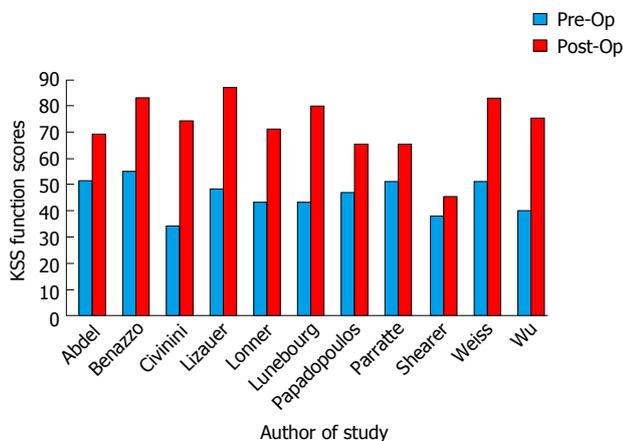


Figure 2 Comparison of pre- and post-operative Knee Society Scores function scores for patients who underwent total knee arthroplasty for treatment of post-traumatic arthritis. KSS: Knee Society Scores; Op: Operative.

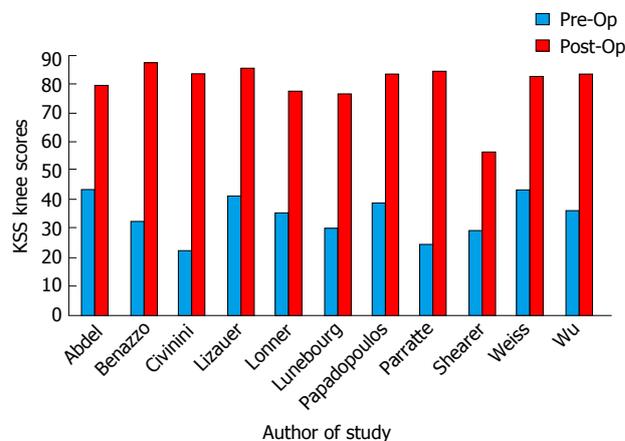


Figure 3 Comparison of pre- and post-operative Knee Society Scores knee scores for patients who underwent total knee arthroplasty for treatment of post-traumatic arthritis. KSS: Knee Society Scores; Op: Operative.

in all five categories - pain, symptoms, activities of daily living, sports activity, and quality of life.

With regards to knee and pain scores, all studies utilizing the KSS criteria showed trends towards or significant improvement in pre- and post-operative scores (Figure 3). Lizaur-Utrilla *et al*^[11] reported no significant difference in post-operative scores between patients with PTA vs primary OA. They also found no significant difference in WOMAC pain scores between the two groups^[11]. Further, Weiss *et al*^[12] examined patient-reported pain. Whereas all patients reported at least mild pain prior to the PTA, 83.9% denied having any pain after the

surgery.

Ten studies examined the effect of TKA on the range of motion (ROM). All studies found an improvement in the mean arc of motion (Figure 4). Arthroplasty provided a substantial gain in flexion^[13]. Some studies further compared the ROM between patients with PTA and primary OA. Lunebourg *et al*^[8] observed that while the degree of improvement in ROM was greater in patients who underwent TKA for PTA, the final results were still significantly lower than those with primary OA. However, Lizaur-Utrilla *et al*^[11] reported no significant difference in the final ROM of patients who underwent TKA for PTA vs

Table 2 Summary of complications observed with total knee arthroplasty for patients with post-traumatic arthritis

Ref.	Total	S Infxn	D Infxn	STIFF	MUA	ROT	WC	O/P	INST	AL	REVR
Abdel <i>et al</i> ^[14]	34	3	5	10	1	1	5	8	3	6	18
Bala <i>et al</i> ^[9]	54	15	1	1	2	1	5	0	1	1	5
Benazzo <i>et al</i> ^[24]	21	1	2	5	1	1	1	1	1	2	7
Civinini <i>et al</i> ^[25]	32	4	4	8	1	4	4	1	1	4	1
Deschamps <i>et al</i> ^[23]	18	1	1	1	1	1	1	1	1	3	13
Lizaur-Utrilla <i>et al</i> ^[11]	14	3	1	1	3	3	3	1	1	3	3
Lonner <i>et al</i> ^[17]	57	1	10	1	1	3	6	1	1	1	1
Lunebourg <i>et al</i> ^[8]	21	1	6	6	1	1	1	1	1	3	9
Massin <i>et al</i> ^[13]	28	5	5	1	1	8	1	1	1	3	5
Papadopoulos <i>et al</i> ^[22]	19	1	6	1	1	2	4	1	2	1	13
Parratte <i>et al</i> ^[19]	26	3	3	8	1	4	1	1	1	1	1
Saleh <i>et al</i> ^[6]	67	1	15	1	20	1	1	7	7	1	1
Scott <i>et al</i> ^[16]	35	13	3	9	1	6	1	1	0	1	1
Shearer <i>et al</i> ^[10]	21	1	4	1	1	1	1	1	6	2	1
Weiss <i>et al</i> ^[12]	26	3	3	10	8	8	5	1	2	2	8
Wu <i>et al</i> ^[26]	47	13	1	1	27	13	1	1	7	1	1

All values are in percents. ¹Denotes the literature did not make mention of this complication, presumably because there were no such cases observed. S Infxn: Superficial infections; D Infxn: Deep infections; STIFF: Stiffness; MUA: Manipulation under anesthesia; ROT: Rupture of tendons; WC: Wound complications; O/P: Osteolysis/polywear; INST: Instability; AL: Aseptic loosening; REVR: Revision rate.

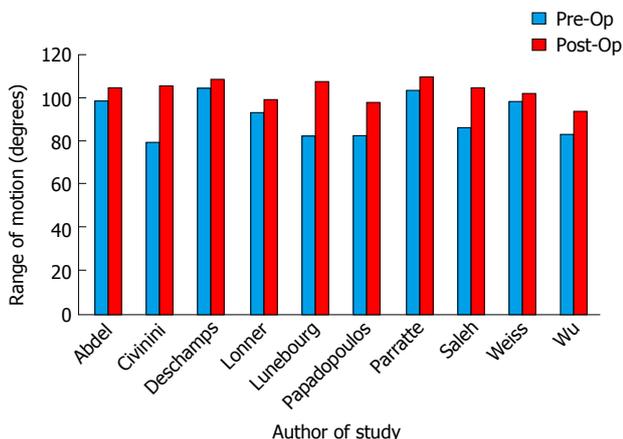


Figure 4 Comparison of average pre- and post-operative range of motions of the knee for patients who underwent total knee arthroplasty for treatment of post-traumatic arthritis. Op: Operative.

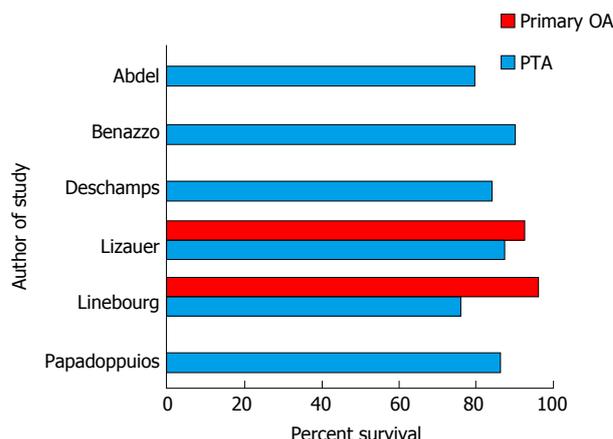


Figure 5 Comparison of survivorship at the longest time of follow-up of total knee arthroplasty performed for post-traumatic arthritis vs primary osteoarthritis. OA: Osteoarthritis; PTA: Post-traumatic arthritis.

primary OA.

Complications

Nine studies examined complications from TKA. The total complication rate at the time of longest follow-up ranged from 14% to 67%. Lizaur-Utrilla *et al*^[11] reported that the complication rate was significantly higher in patients with PTA vs primary OA. The most commonly reported complications included superficial infections, deep infections, stiffness, manipulation under anesthesia (MUA), rupture of tendons, wound complications, osteolysis/polyethylene wear, instability, and aseptic loosening (Table 2). Bala *et al*^[9] further reported that compared to patients with primary OA, patients with PTA had significantly higher complication rates of cellulitis, closed fractures, and wound complications. However, there was no difference between the groups in the rates of bleeding, broken prostheses, mechanical complications, MUA,

osteolysis/polyethylene wear, or rupture of tendons^[9]. In addition, nine studies analyzed the rate of revisions. This ranged from 3% to 18%.

Survivorship

Six studies assessed the survivorship from any revision following TKA. Endpoints were defined as any surgery on the operated knee after the index TKA. Lizaur-Utrilla *et al*^[11], after a mean follow-up of 7 years reported 90% survival, with no significant difference from those with primary OA. After a mean follow-up of 11 years, Lunebourg *et al*^[8] reported a survivorship of 79%, significantly lower than patients with primary OA. Abdel *et al*^[14], after a follow-up of 15 years, reported 82% survival (Figure 5).

DISCUSSION

There is a paucity in the literature regarding the out-

come of TKA performed for the treatment of PTA. This systematic review aimed to examine the current English literature to investigate the clinical outcomes, perioperative complications, and survivorship of TKA for PTA.

Several studies utilized different scoring systems to judge the functional outcomes of TKA in PTA patients. Most of the studies utilized the KSS criteria, which is composed of a functional and knee score. The functional score includes a patient assessment of walking distance, ability to climb stairs, and need for assistive devices; the knee score incorporates patient reported pain, ROM, alignment, and stability^[10]. The overwhelming majority of these studies reported an improvement in the functional and knee scores of patients following TKA for PTA. Lizaur-Utrilla *et al.*^[11] further reported that there were no significant differences in knee or WOMAC pain scores of patients treated with TKA for PTA vs primary OA. Lunebourg *et al.*^[8], while reporting significant improvement in scores, noted lower post-operative scores for patients with PTA vs primary OA.

These results indicate that TKA is an effective treatment for patients with PTA. It results in functional improvement, as well as increased range of motion and reduction in pain. With regards to the lower post-operative scores noted above, despite significant improvement, it is reasonable to infer that this difference compared to patients undergoing TKA for primary OA may be due to differences in the pre-operative status of the patients^[8]. Thus, the post-operative difference observed in patients with PTA vs primary OA, is not due to the intrinsic success of the procedure itself, but rather the poorer pre-operative status of patients with PTA^[8].

Six studies examined the survivorship of TKA with revision for any reason as an end point. Lizaur-Utrilla *et al.*^[11] found no significant difference in survivorship between patients with PTA vs primary OA, whereas Lunebourg did observe a difference^[8]. Perhaps this disparity is due to differences in the lengths of follow-up. With increased length of follow-up, there seems to be a significant difference, in that TKA performed for PTA required more revisions and thus had decreased survivorship, compared to TKA performed for primary OA. Abdel *et al.*^[14] reported that the majority of the TKA revisions were for polyethylene wear. Given that patients with PTA tend to present at a younger age than primary OA, it is reasonable to at least partially attribute the decreased survivorship of TKA in patients with PTA to increased use and wear due to the younger age of this patient group^[12]. Again, the difference in survivorship of TKA may be due to the patient population, and not the intrinsic success of the surgery. For example, Stiehl *et al.*^[15] reported higher risk-adjusted rates of failure in females and younger patients. Further long-term studies are needed to better characterize the factors that affect the survivorship of TKA for PTA.

All sixteen studies reported complications with TKA, including infection, stiffness, wound complications, intraoperative rupture of tendons, and osteolysis/ poly-

ethylene wear. Scott *et al.*^[16] observed no significant difference in the overall rate of complications between patients who underwent TKA for PTA and primary OA. However, the type of complication differed between the two groups; wound complications and stiffness were observed more frequently in patients with TKA^[16]. Abdel *et al.*^[14], even with the longest follow-up time of 15 years, reported that 90% of their complications occurred within the first two years of surgery. This data suggests that perioperative complications are more of a concern than long-term complications of TKA^[14]. Despite the high rate of complications, most did not affect functional outcomes nor require further surgeries^[11].

Many factors likely contribute to this observed rate of complications. First, patients with PTA have an inherent health challenge, in that PTA causes severe joint deformity as it is often accompanied by arthrofibrosis and malunion/nonunion of the fracture^[9]. Second, patients with PTA often have had previous operations, which may compromise the soft-tissue surrounding the knee and thus predispose these patients to infections and wound complications^[12]. Prior fracture surgeries are associated with increased infection rates after TKA^[17]. Piedade *et al.*^[18] reported that prior knee surgery predisposes to higher post-operative complication rates in primary TKA. Third, scarring of the tissue, including fibrosis, may complicate exposure during surgery and positioning of the implant during surgery^[12,19]. Malpositioning has been shown to have a negative effect on the long-term survival of TKA^[20]. Efforts to preserve skin and soft-tissue vascularity, restore limb alignment, and ensure proper positioning may help prevent these complications^[21,22]. Osteotomies may be utilized to correct rotational deformities of the knee^[23]. Regardless, majority of studies reported improvement with total knee arthroplasty, with only few observed complications^[24-26].

There are several limitations to this systematic review. First, there was inconsistency among studies regarding the criteria utilized to assess functional outcomes of TKA. However, this only slightly limited inter-study comparison, as majority of studies did utilize the KSS scoring systems. Second, tibial, patellar, and/or femoral fractures were examined in studies, but the results were grouped in this review. Third, there was a wide range in the average length of follow-up among the studies, from 3 to 15 years. However, this revealed not only short-term but also long-term outcomes. Despite these limitations, this review compiled the available research regarding the efficacy of TKA for the treatment of PTA.

In conclusion, despite the paucity in the literature regarding total knee arthroplasty in the treatment of post-traumatic arthritis, several conclusions may be drawn. TKA is an effective treatment for PTA, as it improves functional outcomes, range of motion, and pain. The accelerated nature of PTA and thus poorer pre-operative status of patients may explain the observed differences in the results of TKA following PTA vs primary OA. There is a significant rate of complications associated with this surgery, majority of which occur in the perioperative

period. Scarring from the initial trauma and prior surgeries, as well as the inherent technical difficulty of the operation, likely contribute to this complication rate.

COMMENTS

Background

With a prevalence of 21%-44% reported in the literature, post-traumatic arthritis (PTA) of the knee occurs following intra- or extra-articular fractures of the proximal tibia, patella, and/or distal femur. After non-operative treatment is exhausted, total knee arthroplasty (TKA) is one of the surgical options. Compared to TKA performed for patients with primary osteoarthritis, TKA performed for PTA is often more technically challenging due to previous surgeries and scarring. There is a paucity in the literature regarding TKA for the treatment of PTA. The goal of this systematic review is to summarize the functional outcomes, complications, and survivorship of TKA performed for the treatment of PTA.

Research frontiers

Several factors contribute to PTA following injury to the knee. These include mechanical imbalance, release of pro-inflammatory cytokines, and nonunions and malunions following fractures. TKA following PTA is often challenging, utilizes more hospital resources, and incurs higher costs.

Innovations and breakthroughs

The number of total knee arthroplasties performed in the United States has been increasing over the years. Newer implants have had great success, improving outcomes while decreasing the need for revisions. However, majority of these studies focus on patients with primary OA, not PTA.

Applications

PTA is prevalent in symptomatic arthritis, mainly in weight-bearing joints such as hips, knees and ankles. These patients have usually had prior surgeries and subsequent scarring, making total knee arthroplasties in this population technically more challenging. Understanding the functional outcomes and complications associated with total knee arthroplasties performed following PTA will help the orthopaedic surgeon in providing appropriate quality of care to this challenging subset of patients.

Peer-review

The manuscript is well written and interesting.

REFERENCES

- 1 **Pickering RD**. Posttraumatic arthritis. *Can Fam Physician* 1984; **30**: 1511-1513 [PMID: 21278962]
- 2 **Brown TD**, Johnston RC, Saltzman CL, Marsh JL, Buckwalter JA. Posttraumatic osteoarthritis: a first estimate of incidence, prevalence, and burden of disease. *J Orthop Trauma* 2006; **20**: 739-744 [PMID: 17106388 DOI: 10.1097/01.bot.0000246468.80635.ef]
- 3 **Larson AN**, Hanssen AD, Cass JR. Does prior infection alter the outcome of TKA after tibial plateau fracture? *Clin Orthop Relat Res* 2009; **467**: 1793-1799 [PMID: 19002742 DOI: 10.1007/s11999-008-0615-7]
- 4 **Furman BD**, Mangiapani DS, Zeitler E, Bailey KN, Horne PH, Huebner JL, Kraus VB, Guilak F, Olson SA. Targeting pro-inflammatory cytokines following joint injury: acute intra-articular inhibition of interleukin-1 following knee injury prevents post-traumatic arthritis. *Arthritis Res Ther* 2014; **16**: R134 [PMID: 24964765 DOI: 10.1186/ar4591]
- 5 **Anderson DD**, Marsh JL, Brown TD. The pathomechanical etiology of post-traumatic osteoarthritis following intraarticular fractures. *Iowa Orthop J* 2011; **31**: 1-20 [PMID: 22096414]
- 6 **Saleh KJ**, Sherman P, Katkin P, Windsor R, Haas S, Laskin R, Sculco T. Total knee arthroplasty after open reduction and internal fixation of fractures of the tibial plateau: a minimum five-year follow-up study. *J Bone Joint Surg Am* 2001; **83-A**: 1144-1148 [PMID: 11507121]
- 7 **Schenker ML**, Mauck RL, Ahn J, Mehta S. Pathogenesis and prevention of posttraumatic osteoarthritis after intra-articular fracture. *J Am Acad Orthop Surg* 2014; **22**: 20-28 [PMID: 24382876 DOI: 10.5435/JAAOS-22-01-20]
- 8 **Lunebourg A**, Parratte S, Gay A, Ollivier M, Garcia-Parra K, Argenson JN. Lower function, quality of life, and survival rate after total knee arthroplasty for posttraumatic arthritis than for primary arthritis. *Acta Orthop* 2015; **86**: 189-194 [PMID: 25350612 DOI: 10.3109/17453674.2014.979723]
- 9 **Bala A**, Penrose CT, Seyler TM, Mather RC, Wellman SS, Bolognesi MP. Outcomes after Total Knee Arthroplasty for post-traumatic arthritis. *Knee* 2015; **22**: 630-639 [PMID: 26526636 DOI: 10.1016/j.knee.2015.10.004]
- 10 **Shearer DW**, Chow V, Bozic KJ, Liu J, Ries MD. The predictors of outcome in total knee arthroplasty for post-traumatic arthritis. *Knee* 2013; **20**: 432-436 [PMID: 23313556 DOI: 10.1016/j.knee.2012.12.010]
- 11 **Lizaur-Utrilla A**, Collados-Maestre I, Miralles-Muñoz FA, Lopez-Prats FA. Total Knee Arthroplasty for Osteoarthritis Secondary to Fracture of the Tibial Plateau. A Prospective Matched Cohort Study. *J Arthroplasty* 2015; **30**: 1328-1332 [PMID: 25795233 DOI: 10.1016/j.arth.2015.02.032]
- 12 **Weiss NG**, Parvizi J, Hanssen AD, Trousdale RT, Lewallen DG. Total knee arthroplasty in post-traumatic arthrosis of the knee. *J Arthroplasty* 2003; **18**: 23-26 [PMID: 12730923 DOI: 10.1054/arth.2003.50068]
- 13 **Massin P**, Bonnin M, Paratte S, Vargas R, Piriou P, Deschamps G. Total knee replacement in post-traumatic arthritic knees with limitation of flexion. *Orthop Traumatol Surg Res* 2011; **97**: 28-33 [PMID: 21167802 DOI: 10.1016/j.otsr.2010.06.016]
- 14 **Abdel MP**, von Roth P, Cross WW, Berry DJ, Trousdale RT, Lewallen DG. Total Knee Arthroplasty in Patients With a Prior Tibial Plateau Fracture: A Long-Term Report at 15 Years. *J Arthroplasty* 2015; **30**: 2170-2172 [PMID: 26195353 DOI: 10.1016/j.arth.2015.06.032]
- 15 **Stiehl JB**, Hamelynck KJ, Voorhorst PE. International multi-centre survivorship analysis of mobile bearing total knee arthroplasty. *Int Orthop* 2006; **30**: 190-199 [PMID: 16547718 DOI: 10.1007/s00264-005-0053-z]
- 16 **Scott CE**, Davidson E, MacDonald DJ, White TO, Keating JF. Total knee arthroplasty following tibial plateau fracture: a matched cohort study. *Bone Joint J* 2015; **97-B**: 532-538 [PMID: 25820894 DOI: 10.1302/0301-620X.97B4.34789]
- 17 **Lonner JH**, Pedlow FX, Siliski JM. Total knee arthroplasty for post-traumatic arthrosis. *J Arthroplasty* 1999; **14**: 969-975 [PMID: 10614889]
- 18 **Piedade SR**, Pinaroli A, Servien E, Neyret P. TKA outcomes after prior bone and soft tissue knee surgery. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2737-2743 [PMID: 22829329 DOI: 10.1007/s00167-012-2139-7]
- 19 **Parratte S**, Boyer P, Piriou P, Argenson JN, Deschamps G, Massin P. Total knee replacement following intra-articular malunion. *Orthop Traumatol Surg Res* 2011; **97**: S118-S123 [PMID: 21872547 DOI: 10.1016/j.otsr.2011.07.001]
- 20 **Suzuki G**, Saito S, Ishii T, Motojima S, Tokuhashi Y, Ryu J. Previous fracture surgery is a major risk factor of infection after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 2040-2044 [PMID: 21541707 DOI: 10.1007/s00167-011-1525-x]
- 21 **Lotke PA**, Ecker ML. Influence of positioning of prosthesis in total knee replacement. *J Bone Joint Surg Am* 1977; **59**: 77-79 [PMID: 833180]
- 22 **Papadopoulos EC**, Parvizi J, Lai CH, Lewallen DG. Total knee arthroplasty following prior distal femoral fracture. *Knee* 2002; **9**: 267-274 [PMID: 12424033]
- 23 **Deschamps G**, Khiami F, Catonné Y, Chol C, Bussi re C, Massin P. Total knee arthroplasty for osteoarthritis secondary to extra-articular malunions. *Orthop Traumatol Surg Res* 2010; **96**: 849-855 [PMID: 21035414 DOI: 10.1016/j.otsr.2010.06.010]
- 24 **Benazzo F**, Rossi SM, Ghiara M, Zanardi A, Peticarini L, Combi

- A. Total knee replacement in acute and chronic traumatic events. *Injury* 2014; **45** Suppl 6: S98-S104 [PMID: 25457327 DOI: 10.1016/j.injury.2014.10.031]
- 25 **Civinini R**, Carulli C, Matassi F, Villano M, Innocenti M. Total knee arthroplasty after complex tibial plateau fractures. *Chir Organi Mov* 2009; **93**: 143-147 [PMID: 19711154 DOI: 10.1007/s12306-009-0033-3]
- 26 **Wu LD**, Xiong Y, Yan SG, Yang QS. Total knee replacement for posttraumatic degenerative arthritis of the knee. *Chin J Traumatol* 2005; **8**: 195-199 [PMID: 16042863]

P- Reviewer: Anand A, Jiao C, Willis-Owen CA
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Li D



Biologic agents for anterior cruciate ligament healing: A systematic review

Berardo Di Matteo, Markus Loibl, Luca Andriolo, Giuseppe Filardo, Johannes Zellner, Matthias Koch, Peter Angele

Berardo Di Matteo, Luca Andriolo, Giuseppe Filardo, I Orthopaedic and Traumatologic Clinic - Biomechanics and Technology Innovation Laboratory, Rizzoli Orthopaedic Institute, 40136 Bologna, Italy

Markus Loibl, Johannes Zellner, Matthias Koch, Peter Angele, Department of Trauma Surgery, University Regensburg Medical Centre, 93042 Regensburg, Germany

Peter Angele, Sporthopaedicum Regensburg, 93053 Regensburg, Germany

Author contributions: Di Matteo B, Andriolo L, Filardo G and Koch M were responsible for the literature research and for collecting the data and preparing the figures and tables included in the manuscript; Di Matteo B, Loibl M, Zellner J and Angele P wrote the paper; Loibl M and Angele P were responsible for the critical revision of the entire manuscript.

Conflict-of-interest statement: No conflict of interest to declare for the present paper.

Data sharing statement: All the source data used to perform the present systematic review are available from the corresponding author at berardo.dimatteo@gmail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Berardo Di Matteo, MD, I Orthopaedic and Traumatologic Clinic - Biomechanics and Technology Innovation Laboratory, Rizzoli Orthopaedic Institute, Via Pupilli n. 1, 40136 Bologna, Italy. berardo.dimatteo@gmail.com
Telephone: +39-051-6366567
Fax: +39-051-583789

Received: April 20, 2016

Peer-review started: April 22, 2016

First decision: June 6, 2016

Revised: June 22, 2016

Accepted: July 14, 2016

Article in press: July 18, 2016

Published online: September 18, 2016

Abstract

AIM

To systematically review the currently available literature concerning the application of biologic agents such as platelet-rich plasma (PRP) and stem cells to promote anterior cruciate ligament (ACL) healing.

METHODS

A systematic review of the literature was performed on the use of biologic agents (*i.e.*, PRP or stem cells) to favor ACL healing during reconstruction or repair. The following inclusion criteria for relevant articles were used: Clinical reports of any level of evidence, written in English language, on the use of PRP or stem cells during ACL reconstruction/repair. Exclusion criteria were articles written in other languages, reviews, or studies analyzing other applications of PRP/stem cells in knee surgery not related to promoting ACL healing.

RESULTS

The database search identified 394 records that were screened. A total of 23 studies were included in the final analysis: In one paper stem cells were applied for ACL healing, in one paper there was a concomitant application of PRP and stem cells, whereas in the remaining 21 papers PRP was used. Based on the ACL injury pattern, two papers investigated biologic agents in ACL partial tears whereas 21 papers in ACL reconstruction. Looking at the quality of the available literature, 17 out of 21 studies dealing with ACL reconstruction were randomized controlled trials. Both studies on ACL repair were case series.

CONCLUSION

There is a paucity of clinical trials investigating the role of stem cells in promoting ACL healing both in case of partial and complete tears. The role of PRP is still controversial and the only advantage emerging from the literature is related to a better graft maturation over time, without documenting beneficial effects in terms of clinical outcome, bone-graft integration and prevention of bony tunnel enlargement.

Key words: Platelet-rich plasma; Growth factors; Stem cells; Anterior cruciate ligament reconstruction; Anterior cruciate ligament repair; Anterior cruciate ligament healing; Sports medicine; Regenerative medicine

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: There has been a growing interest in the past years on regenerative approaches to stimulate healing of musculo-skeletal tissues. The present systematic review focuses on the clinical application of biologic agents [platelet-rich plasma (PRP) and stem cells] to favor anterior cruciate ligament healing during procedures of reconstruction or repair. We show that there is inconclusive evidence to support the use of biologic augmentations, also due to the paucity of trials currently available, especially concerning stem cells. Looking at PRP, positive findings in terms of promotion of graft maturation were documented, but no beneficial influence was observed in terms of clinical outcome, bone-graft integration and prevention of tunnel enlargement.

Di Matteo B, Loibl M, Andriolo L, Filardo G, Zellner J, Koch M, Angele P. Biologic agents for anterior cruciate ligament healing: A systematic review. *World J Orthop* 2016; 7(9): 592-603 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/592.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.592>

INTRODUCTION

Anterior cruciate ligament (ACL) injuries are among the most common conditions treated in everyday orthopaedic practice, with an increasing incidence in the past years due to a concurrent increase of sports activities among the general population^[1,2]. ACL lesions can be distinguished in complete tears, generally treated by reconstruction, and partial tears (*i.e.*, incomplete tears of one or both ACL bundles). Their management can be very challenging, ranging from non-operative treatment to surgery (augmentation or traditional reconstruction), depending on the patients' symptoms and functional needs^[3]. Epidemiological studies reveal an average incidence of 30 ACL injuries per 100000 people annually. Every year 175000 patients undergo ACL reconstruction in the United States^[4]. These numbers highlight the social and economical impact of ACL injuries, and therefore justify the large interest in optimizing the treatment

strategies for this particular injury. Several reconstructive techniques have been proposed in the past decades, mainly differing in terms of graft selection and graft fixation. The overall results are quite satisfactory, even at long-term evaluation, without a difference in terms of outcome among different surgical techniques^[5,6]. Nevertheless, a documented failure rate of up to 14% for ACL reconstruction^[7], stimulates scientific efforts to find solutions that could promote better graft maturation and healing to minimize the risk of failure and to allow a faster recovery for patients. Beyond maximizing the results of ACL reconstruction, there is an increasing demand for minimally invasive options to enhance intrinsic ACL healing in case of partial ruptures. These injuries represent a substantial amount of ACL injuries, whose treatment algorithm is still controversial. The possibility of promoting ACL healing without reconstruction is regarded as an attractive perspective, due to the inherent lower surgical morbidity and the faster return to physical activities.

The recent progress in the field of regenerative medicine has led to the application of biologic agents (platelet-derived growth factors and stem cells), which could provide a positive stimulus to tissue healing. Platelet-rich plasma (PRP) is currently the most exploited biological augmentation used in orthopaedic practice, both for the treatment of degenerative disease (like osteoarthritis and tendinopathies), and sports-related injuries^[8,9]. It is an autologous blood derived product which is obtained by centrifugation or filtration of peripheral blood in order to concentrate platelets, which are a reservoir of several growth factors and bioactive molecules involved in tissue homeostasis and anabolism^[10,11]. Several *in vitro* and animal studies demonstrated that intra-ligamentary administration of PRP determines an increase in cellular density and neovascularization of the ACL. This results in a better organization of collagen fibers for superior tensile resistance and biomechanical properties^[12-14]. In light of these promising pre-clinical data, and also due to the easy preparation modalities, platelet-rich products are used more and more by clinicians from all over the world. In more recent times, mesenchymal stem cells from different sources have been proposed to augment ACL reconstruction or repair. In this case, flourishing pre-clinical literature suggests that stem cell administration could stimulate tissue maturation, improve histological appearance, and favor bone-to-tendon integration^[15,16]. Therefore, the implementation of experimental techniques in the clinical practice seems reasonable. A relevant number of clinical reports have been published investigating the actions of these fashionable biological strategies so far. The aim of the present paper is to systematically review the available literature concerning the application of PRP or stem cells to stimulate ACL healing, and to trace the state of the art in the use of biologic agents in this particular field of sports medicine. Moreover, this paper reveals if these novel strategies could really play a beneficial role in promoting graft maturation and healing and provide a better clinical outcome in the treatment of

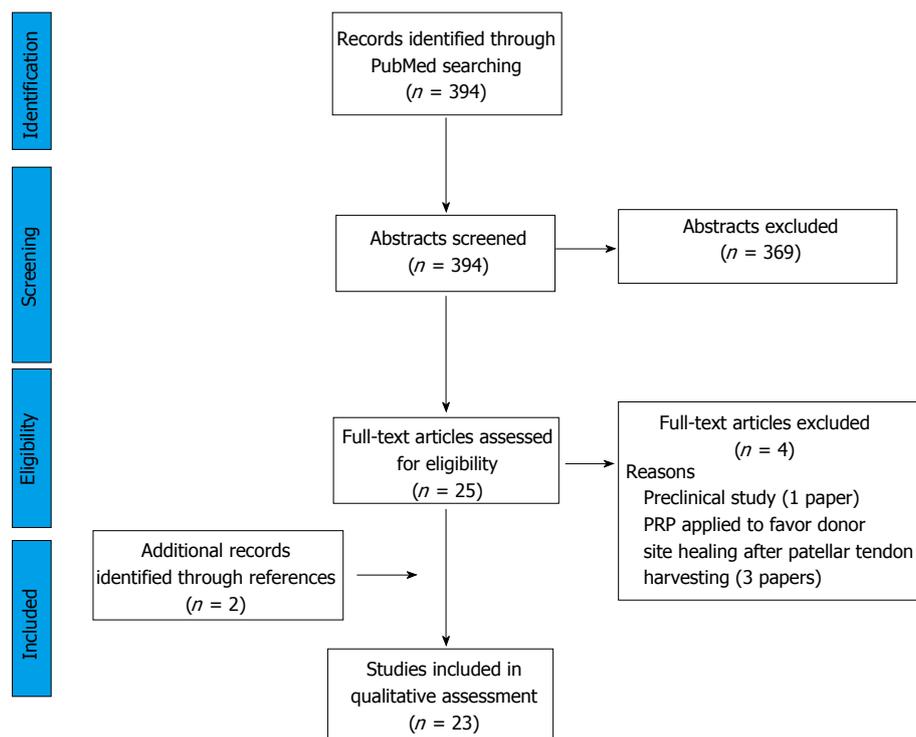


Figure 1 PRISMA flowchart resuming the papers' selection process. PRP: Platelet-rich plasma.

complete and partial ACL lesions.

MATERIALS AND METHODS

A systematic review of the literature was performed on the use of biologic agents (*i.e.*, PRP or stem cells) to promote ACL healing during surgical reconstruction or repair. The search was conducted on the PubMed database on March 31, 2016 using the following formula: [(PRP or platelet concentrate or platelet gel or platelet rich plasma or ACP or autologous conditioned plasma or PRGF or PRF or platelet lysate or platelet derived growth factors or plasma growth factors or platelet rich fibrin) or (stem cell or mesenchymal or mesenchymal stem cell or bone marrow concentrate or bone marrow aspirate or adipose derived or peripheral blood)] and (ACL or anterior cruciate ligament).

Screening process and analysis were conducted separately by two independent observers (Di Matteo B and Andriolo L). First, the articles were screened by title and abstract. The following inclusion criteria for relevant articles were used during the initial screening of titles and abstracts: Clinical reports of any level of evidence, written in English language, published in the past 20 years (1996-2016), on the use of PRP or stem cells during ACL reconstruction/repair. Exclusion criteria were articles written in other languages, reviews, or studies analyzing other applications of PRP/stem cells in knee surgery not related to promoting ACL healing. In the second step, the full texts of the selected articles were screened, with further exclusions according to the previously described criteria. Moreover, the articles not reporting clinical, magnetic resonance imaging (MRI), or

histologic results were excluded. Reference lists from the selected papers were also screened. A flowchart of the systematic review is provided in Figure 1. Relevant data were then extracted and collected in a unique database, with the consensus of the two observers, to be analyzed for the purposes of the present manuscript.

RESULTS

Qualitative synthesis of trials included in the review

The database search identified 394 records, and the abstracts were screened and selected according to the inclusion/exclusion criteria. As shown in Figure 1, a total of 27 full-text articles were assessed for eligibility. Four articles did not fulfill the inclusion criteria and were further excluded, leading to a total of 23 studies included in the final analysis (Figure 1). Only one paper dealt with the application of stem cells for ACL healing^[17], one paper investigated the concurrent action of PRP and stem cells^[18], whereas the remaining 21 papers focused on PRP application solely (one in partial rupture and 20 in ACL reconstruction)^[19-39]. Based on the ACL injury pattern, two papers investigated biologic agents in ACL partial tears^[18,19] whereas 21 papers in ACL reconstruction^[17,20-39].

Looking at the quality of the available literature, 17 out of 21 studies dealing with ACL reconstruction were randomized controlled trials (RCTs) (Table 1), whereas only case series are available for ACL repair.

Concerning delivery methods of biologic agents, several different strategies were tested by authors, sometimes in combination (Table 1): Simple intra-articular injection, intra-ligamentary injection, local

application onto the surface of the tendon graft, local injection within the bony tunnels, multiple intra-tendinous depots, or even selective administration through a spongy membrane soaked in PRP and sutured around the graft.

The different application methods will be discussed separately according to the specific ACL treatment analyzed in the clinical trials, *i.e.*, repair (2 studies) or reconstruction (21 studies). A detailed description of the trial features is presented in Table 1.

Biologic agents in ACL repair

Two papers investigated the contribution of biologic agents applied to promote healing of ACL in case of partial rupture. The first one, a retrospective case series, was published by Seijas *et al.*^[19] in 2014. They analyzed a small cohort of 19 football players who were treated by arthroscopic intra-ligamentary injection of 4 mL of leukocyte-poor PRP, followed by a 6 mL intra-articular injection at the end of surgery. The results were pretty satisfactory and 16 out of 19 patients were able to return to previous sports activity level with stable knees (evaluated by KT-1000), and in particular patients with Tegner Score 10 achieved the fastest return to sports. In the prospective trial published by Centeno *et al.*^[18], ten patients in total were treated by fluoroscopic guided intra-ligamentary injection of PRP + platelet lysate + bone marrow derived stem cells (harvested from the iliac crest and concentrated in the operating room). Overall results were satisfactory, with seven out of ten patients presenting signs of ACL healing at MRI evaluation performed at average 3 mo from the procedure. This evidence suggested a potential clinical usefulness of this approach to be confirmed by a larger trial.

Biologic agents in ACL reconstruction

Twenty-one papers^[17,20-39] investigated the role of biologic agents during ACL reconstruction; only one paper dealt^[17] with the use of bone marrow concentrate, whereas 19 focused on PRP. With regards to the graft used for reconstruction, in 14 trials authors employed hamstrings, in three patellar tendon, in two trials ACLs were either reconstructed with hamstrings or patellar tendon, and just one paper documented the use of allograft. The papers published analyzed the following main outcomes after biologic agents administration (Table 1): (1) clinical results evaluated by functional scores, objective measurements and time to return to sports; (2) bony tunnel enlargement over time [evaluated by computed tomography (CT)]; (3) ACL graft-bone interface integration (evaluated by MRI); and (4) ACL graft maturation/remodeling (evaluated by MRI).

Looking at clinical outcomes and functional scores, eight papers^[20-27] analyzed this specific aspect, seven of which were RCTs. Overall results were controversial: The RCTs authored by Del Torto *et al.*^[21], Darabos *et al.*^[22] and Vogrin *et al.*^[23] showed significant advantage of PRP administration over the control group. In particular, Del Torto *et al.*^[21] documented superior clinical outcome (IKDC subjective score) for the PRP group at any follow-

up evaluation up to 24 mo; similar results were reported by Darabos *et al.*^[22], who documented less swelling and better performance in functional tests at 6 mo, and also a significant difference in WOMAC Stiffness subscale at 12 mo. Interestingly, also a reduced synovial fluid concentration of IL-1b was found in the PRP group after 10 d from the procedure. Vogrin *et al.*^[23] reported a significant difference in favor of PRP when comparing KT-2000 values at 3 and 6 mo after surgery. It was suggested that growth factors played a substantial role in enhancing knee stability. Conversely, four RCTs^[24-27] were not able to document any clinical benefit from PRP administration. In particular the trial authored by Valentí Azcárate *et al.*^[24] included 150 patients divided into three treatment groups and evaluated up to 24 mo. Two different PRP formulations (PRGF and lab made PRP) were tested without demonstrating any clinical benefit over control groups, either in terms of objective or subjective measurements, with the exception of swelling, which was observed to be less 24 h after surgery in the PRGF group compared to PRP and control groups.

The issue of prevention of bony tunnels enlargement was addressed in six trials, all of which were RCTs^[22,25,28-31]. Only in two of them^[22,28] it was demonstrated that PRP, injected locally into the tunnels^[28] or intra-articularly^[22], could prevent their enlargement over time. Conversely, four papers revealed no significant difference with regard to this specific outcome between treatment groups. Additionally, one paper^[31] revealed that the only positive effect in preventing tunnel widening was achieved by implanting a bone plug into the tunnel.

Concerning the graft-bone tunnel integration, eight papers (six RCTs)^[17,21,24,31-35] investigated this specific issue. In only two RCTs the use of PRP provided beneficial effects in terms of better corticalization of the tunnel walls^[32] or higher vascularization at the graft-bone interface^[33], whereas in the remaining trials^[17,21,24,31,34,35] no inter-group difference was observed over time. Among the papers reporting negative results for PRP in this specific parameter, there is also only one study^[17] documenting the role of bone marrow concentrate, which was not able to provide beneficial effects.

Diverging results were reported when analyzing the graft maturation over time after ACL reconstruction. Eight papers in total (five RCTs)^[27,31,33,34,36-39] assessed this specific parameter, and six of them (four RCTs) documented a positive influence of PRP administration^[27,31,36-39], whereas just two papers (one RCT) failed to reveal any inter-group difference^[33,34]. In the vast majority of cases graft maturation was evaluated by imaging assessment, revealing a helpful role of PRP in stimulating a faster and better MRI or CT appearance of the graft. Signal of the graft was more similar to the posterior cruciate ligament, which points out an overall positive modulation of the ligamentization process. One paper^[39] reported also histologic evaluation of the grafts, which were biopsied during second look arthroscopies performed after a mean of 15 mo from primary ACL reconstruction. In the PRP group, the graft presented a significantly better

Table 1 Synopsis of all clinical trials dealing with the application of biologic agents to promote anterior cruciate ligament healing

Ref.	Study design	Methods	Results
Clinical results			
+ Del Torto <i>et al</i> ^[21]	Prospective comparative study (PRFM vs control) 28 patients (14 vs 14)	ACL reconstruction with hamstring tendon graft fixed in the femoral tunnel through the RIGIDFIX system (DePuy) and in the tibial tunnel through the Bio-INTRAFIX system (DePuy) PRFM was prepared using Cascade Medical Enterprises 2 tube kit (Cascade Medical Enterprises, Wayne, NJ). PRFM clot was sutured in the proximal graft loop and it reaches the proximal tunnel once the graft is pulled in place. Distally, the PRFM clot was inserted between the four strands of the G-ST graft before the interference screw system was applied	PRFM-augmented patients showed a statistically significant higher clinical improvement at 24 mo follow-up ($P = 0.032$) Objective clinical evaluation both through IKDC score and with Rolimeter arthrometer did not show any difference between the two groups
Magnussen <i>et al</i> ^[20]	Retrospective comparative study (PRP vs control) 58 patients (29 vs 29)	ACL reconstruction with allograft tibial tendon, fixed with absorbable cross pin in femoral tunnel and absorbable interference screw in tibial tunnel After graft positioning, intra-articular portion was coated with PRP prepared with GPS II Platelet Concentrate Separation Kit (Biomet)	Decreased effusions at 10 ± 4 d was noted in the PRP group, but this difference disappeared by 8 ± 4 wk No differences in patient-reported outcomes were noted in the 58 patients with two-year outcome data
Darabos <i>et al</i> ^[22]	Randomized trial (ACS vs control) 62 patients (31 vs 31)	ACL reconstruction with hamstring (30) or patellar tendon (32), fixed with BioTransFix (Arthrex) or RigidFix (Mytek) at femoral side, and with an interference screw at the tibial side ACS was produced drawing venous blood into syringes containing pre-treated glass beads, and after a period of incubation serum is extracted through centrifugation. ACS was administered with an injection regime of 4 injections on day 0 (day of surgery), day 1, day 6, and day 10	Clinical outcomes were consistently better in patients treated with ACS at all data points and for all outcome parameters, with statistically significant differences in the WOMAC stiffness subscale after 1 yr Decrease in IL-1b synovial fluid concentration was more pronounced in ACS group, with statistically significant lower values in the ACS group at day 10
Vogrin <i>et al</i> ^[23]	Randomized trial (PRP vs control) 45 patients (22 vs 23)	ACL reconstruction with double-looped semitendinosus and gracilis tendon graft fixed with two bioabsorbable cross pins in the femoral tunnel and one bioabsorbable interference screw in the tibial tunnel PRP was produced with Magellan system (Medtronic) and applied into the femoral and tibial tunnels as well as onto the graft itself	PRP group demonstrated significantly better anteroposterior knee stability than control group: Calculated improvements in knee stability at 6 mo were 1.3 ± 1.8 mm in the control group and 3.1 ± 2.5 mm in the platelet gel group ($P = 0.011$)
- Valentí Azcárate <i>et al</i> ^[24]	Randomized trial (PRP vs PRGF vs control) 150 patients (50 vs 50 vs 50)	ACL reconstruction using a patellar tendon allograft transtibial technique fixed with a RigidFix technique (DePuy Mitek,) with two biodegradable cross pins at the femoral bone and a tibial biodegradable (Byocril) interference screw PRP was produced with a double-spin procedure using a standard centrifuge and applied covering the ligament and suturing it over itself with gel in its interior, and introducing the gel obtained after activating the poor platelet concentration after implantation of the graft inside the tibial tunnel PRP was produced following Anitua's technique (PRGF-Endoret Technology) and applied injecting it into the graft before implantation, with the biocompatible fibrin applied into the tibial tunnel at the end of surgery	No significant differences in functional results at the final follow-up of 24 m No statistically significant differences between the three groups in CRP 1 and VAS 24 h after surgery No significant differences in the range of knee motion, muscle torque, KT-1000 or IKDC score The PRGF group showed a statistically significant improvement in swelling scores 24 h after surgery compared with the PRP and control groups
Vadalà <i>et al</i> ^[25]	Randomized trial (PRP vs control) 40 patients (20 vs 20)	ACL reconstruction with hamstrings (Out-In technique), fixed with Swing-Bridge device on femoral side and Evolgate screw on tibial side PRP was produced with Fast Biotech kit (MyCells PPT-Platelet Preparation Tube) and applied as follows: 5 mL between peripheral part of the graft and the femoral tunnel wall; 5 mL in semisolid pattern above the graft; 5 mL of liquid and semisolid PRP on the tibial side	Physical examination as well as the evaluation scales used showed no differences between the two groups at 14.7 mo of follow-up
Nin <i>et al</i> ^[26]	Randomized trial (PRP vs control) 100 patients (50 vs 50)	ACL reconstruction with patellar tendon allograft, fixed with two biodegradable cross pins in femur and a tibial biodegradable interference screw Ligament was covered with PRP (produced with standard centrifuge) and sutured over itself with PRP in its interior. The rest of the gel was introduced after implantation of the graft inside the tibial tunnel	The results did not show any statistically significant differences between the groups for inflammatory parameters, magnetic resonance imaging appearance of the graft, and clinical evaluation scores after 18 mo

Ventura <i>et al.</i> ^[27]	Randomized trial (PRP vs control) 20 patients (10 vs 10)	ACL reconstruction with quadruple hamstring tendon graft, with a femoral transcondylic fixation (BioTransFix) and tibial interference screw (BioRCL, Smith and Nephew) PRP was obtained according to the GPS Biomet-Merck technique (Biomet) and applied in femoral and tibial tunnels	There were no significant differences concerning clinical score and examination between the two groups 6 mo after ACL surgery
Tunnel enlargement + Starantzis <i>et al.</i> ^[28]	Randomized trial (PRP vs control) 51 patients (25 vs 26)	ACL reconstruction with hamstring tendons (Semitendinosus and Gracilis) as a quadrupled graft, using distal fixation in the femur (Crosspin Linvatec or Endobutton Linvatec) and tibial fixation with a biodegradable interference screw (Linvatec) plus bone bridge suture anchoring Half of the PRP (produced using the Biomet GPS III kit) was added between the strands of the graft and left to form a clot before the graft fixation. Then, the remaining 3 mL was injected into the femoral tunnel using an introducer	The morphology of the dilated tunnels was conical in both groups There was a statistical significant difference in the mid distance of the tunnels between the two groups 1 yr after surgery No significant difference of the Lysholm scores between the two groups during the observation period was detected
Darabos <i>et al.</i> ^[22]	Randomized trial (ACS vs control) 62 patients (31 vs 31)	ACL reconstruction with hamstring (30) or patellar tendon (32), fixed with BioTransFix (Arthrex) or RigidFix (Mytek) at femoral side, and with an interference screw at the tibial side ACS was produced drawing venous blood into syringes containing pre-treated glass beads, and after a period of incubation serum was extracted through centrifugation. ACS was administered with an injection regime of four injections on day 0 (day of surgery), day 1, day 6, and day 10	Bone tunnel enlargement measured with CT scans was significantly less (6 mo: 8%, 12 mo: 13%) in ACS group than in control group (6 mo: 31%, 12 mo: 38%)
- Vadalà <i>et al.</i> ^[25]	Randomized trial (PRP vs control) 40 patients (20 vs 20)	ACL reconstruction with hamstrings (Out-In technique), fixed with Swing-Bridge device on femoral side and Evolgate screw on tibial side PRP was produced with Fast Biotech kit (MyCells PPT-Platelet Preparation Tube) and applied as follows: 5 mL between peripheral part of the graft and the femoral tunnel wall; 5 mL in semisolid pattern above the graft; 5 mL of liquid and semisolid PRP on the tibial side	The use of PRP did not seem to be effective in preventing tunnel enlargement at 14.7 mo of follow-up
Mirzatooei <i>et al.</i> ^[29]	Randomized trial (PRP vs control) 46 patients (23 vs 23)	ACL reconstruction with single-bundle quadrupled autograft of hamstrings, fixed with a cross-pin in femoral tunnel and a bio-absorbable interference screw in tibial tunnel Graft was immersed in the PRP solution (produced with Double syringe system, Arthrex) for five minutes before implantation; 2 mL of PRP was injected into the femoral tunnel and 1.5 mL into the tibial tunnel at the end of the surgery	Despite slightly less tunnel widening in the PRP group, there were no significant differences at any of the sites of measurement between immediately after surgery and three months post-operatively
Silva <i>et al.</i> ^[30]	Randomized trial (4 groups) 40 patients (10 control vs 10 PRP in FT vs 10 PRP in FT and intra-articular at 2- and 4 wk vs 10 PRP activated with thrombin in FT)	Double-bundle arthroscopic ACL reconstruction with autologous hamstring tendons, fixed with two Endobuttons for the AMT and PLT in the femur and two bioabsorbable interference screws in the tibia PRP (produced with GPS III Kit, Biomet) was placed between the strands of the graft in each femoral tunnel	At 3 mo postoperatively, all tunnels had enlarged compared to the diameter of the drill and most tunnels enlarged more in the midsection than at the aperture in a fusiform manner The use of growth factors during and after surgery did not show any influence in the tunnel enlargement ($P = 0.563$)
Orrego <i>et al.</i> ^[31]	Randomized trial (4 groups) 108 patients (27 control vs 26 PC vs 28 BP vs 27 PC + BP)	ACL reconstructions with quadruple semitendinosus-gracilis graft, fixed with a biodegradable transfixing pin proximally and a biodegradable interference screw distally; BP was placed by interference fit at the femoral tunnel Five milliliter PRP (produced with Biomet GPS II kit, Biomet) was added between the graft strands before passing it into the tunnel. After fixation, 1 mL of PRP was injected into the femoral tunnel between the graft strands	The use of PC did not show any significant effect in the tunnel widening evolution at 6 mo follow-up The use of a BP effectively prevented tunnel widening The BP and PC combination did not show a synergic effect as compared to PC or BP individually
ACL graft-bone interface/integration + Ruprecht <i>et al.</i> ^[32]	Randomized trial (PRP vs control) 41 patients (21 vs 20)	ACL reconstruction with double-looped semitendinosus and gracilis tendon autograft, fixed with two bioabsorbable cross pins in femoral tunnel and one bioabsorbable interference screw in tibial tunnel. PRP was applied after autograft positioning, into the femoral and tibial tunnels (1 mL in each of them), and onto the graft itself (3 mL)	A gradual increase in the percentage of the tunnel wall consisting of tunnel wall cortical bone (TCB) during the follow-up was observed. At 6 mo the mean percentage of TCB was significantly higher ($P = 0.003$) in the PRP group than in the control group

Vogrin <i>et al</i> ^[33]	Randomized trial (PRP vs control) 41 patients (21 vs 20)	ACL reconstruction with double-looped semitendinosus and gracilis tendon graft fixed with two bioabsorbable cross pins in the femoral tunnel and one bioabsorbable interference screw in the tibial tunnel PRP was produced with Magellan system (Medtronic) and applied into the femoral and tibial tunnels as well as onto the graft itself	After 4-6 wk, there was a significantly higher level of vascularization in the osteoligamentous interface in PRP group (0.33 ± 0.09 vs 0.16 ± 0.09, <i>P</i> < 0.001) In the intra-articular part of the graft, there was no evidence of revascularization in either group
- Del Torto <i>et al</i> ^[21]	Prospective comparative study (PRFM vs control) 28 patients (14 vs 14)	ACL reconstruction with hamstring tendon graft fixed in the femoral tunnel through the RIGIDFIX system (DePuy) and in the tibial tunnel through the Bio-INTRAFIX system (DePuy) PRFM was prepared using Cascade Medical Enterprises 2 tube kit (Cascade Medical Enterprises). PRFM clot was sutured in the proximal graft loop and it reaches the proximal tunnel once the graft is pulled in place. Distally, the PRFM clot was inserted between the four strands of the G-ST graft before the interference screw system was applied	MRI evaluation considering graft-tunnel interface and graft signal intensity provided similar results between the two examined groups, without any statistically significant difference. In the majority of the cases, a good signal quality of the graft and a scarce film of synovial fluid at the graft-tunnel interface were observed
Silva <i>et al</i> ^[17]	Randomized trial (BMC vs control) 43 patients (20 vs 23)	ACL reconstruction with double-looped semitendinosus and gracilis tendon autograft fixed with a Toggleloc Ziploop (Biomet) in femoral tunnel and a bioabsorbable interference screw (Biomet) in tibial tunnel Bone marrow was harvested from the iliac crest and concentrated to obtain 3 mL BMC. 1.5 mL of BMC concentrate was injected inside the femoral end of the graft itself before graft positioning, and the remaining 1.5 mL BMC injected within the tunnel around the graft, from the bottom down to the entrance of the tunnel	Adult non-cultivated BMC did not seem to accelerate graft-to-bone healing in ACL reconstruction: No difference in the signal-to-noise ratio of the inter-zone on MRI between the experimental and the control group 3 mo after surgery
Valentí Azcárate <i>et al</i> ^[24]	Randomized trial (PRP vs PRGF vs control) 150 patients (50 vs 50 vs 50)	ACL reconstruction using a patellar tendon allograft transtibial technique fixed with a RigidFix technique (DePuy Mitek) with two biodegradable cross pins at the femoral bone and a tibial biodegradable (Byocril) interference screw PRP was produced with a double-spin procedure using a standard centrifuge and applied covering the ligament and suturing it over itself with gel in its interior, and introducing the gel obtained after activating the poor platelet concentration after implantation of the graft inside the tibial tunnel PRP was produced following Anitua's technique (PRGF-Endoret Technology) and applied injecting it into the graft before implantation, with the biocompatible fibrin applied into the tibial tunnel at the end of surgery	No statistically significant differences were noted between groups in intensity, thickness, or uniformity of graft at 6 mo MRI
Figueroa <i>et al</i> ^[34]	Comparative study (PRP vs control) 50 patients (30 vs 20)	ACL reconstruction with hamstring tendons fixed with a cross-pin in femoral tunnel and a bio-absorbable interference screw in tibial tunnel PRP was produced with Magellan system (Medtronic) and applied under arthroscopy in both the tibial (3 mL) and femoral (3 mL) tunnels with a long needle syringe, and directly applied in the intra-articular graft portion (4 mL)	No statistically significant benefit in the PRP group in terms of integration assessment at 6 mo follow-up
Silva <i>et al</i> ^[35]	Randomized trial (4 groups) 40 patients (10 control vs 10 PRP in FT vs 10 PRP in FT and intra-articular at 2- and 4 wk vs 10 PRP activated with thrombin in FT)	Double-bundle arthroscopic ACL reconstruction with autologous hamstring tendons, fixed with two Endobuttons for the AMT and PLT in the femur and two bioabsorbable interference screws in the tibia PRP (produced with Mini GPS III Kit, Biomet) was placed between the strands of the graft in each femoral tunnel	The graft integration was not complete at 3 mo after surgery in the PL and AM femoral tunnel, and the use of PRP isolated or with thrombin seemed not to accelerate tendon integration
Orrego <i>et al</i> ^[31]	Randomized trial (4 groups) 108 patients (27 control vs 26 PC vs 28 BP vs 27 PC + BP)	ACL reconstructions with quadruple semitendinosus-gracilis graft, fixed with a biodegradable transfixing pin proximally and a biodegradable interference screw distally; BP placed by interference fit at the femoral tunnel 5 mL PRP (produced with GPS II kit, Biomet) was added between the graft strands before passing it into the tunnel. After fixation, 1 mL of PRP was injected into the femoral tunnel between the graft strands	The use of PC did not show any significant effect in the osteoligamentous interface at 6 mo follow-up

ACL graft remodeling

+ Seijas <i>et al</i> ^[36]	Randomized trial (PRP vs control) 98 patients (49 vs 49)	ACL reconstruction with autologous patellar tendon grafts with 9 mm bone plugs and fixed with hydroxyapatite screws in femur and tibia 8 mL of PRP was produced with PRGF technique (BTI Systems Vitoria, Spain) and percutaneously injected into the suprapatellar joint after portal suture	More patients in the PRP group than controls attained higher stages of remodeling at month 4 ($P = 0.003$), month 6 ($P = 0.0001$), and month 12 (but NS $P = 0.354$)
Ruprecht <i>et al</i> ^[37]	Randomized trial (PRP vs control) 41 patients (21 vs 20)	ACL reconstruction with double-looped semitendinosus and gracilis tendon autograft, fixed with two bioabsorbable cross pins in femoral tunnel and one bioabsorbable interference screw in tibial tunnel PRP was applied after autograft positioning, into the femoral and tibial tunnels (1 mL in each of them), and onto the graft itself (3 mL)	MRI measurements indicated a reduced extent of edema during the first postoperative month as well as an increased vascular density and microvessel permeability in the proximal tibial tunnel at 1 and 2.5 postoperative months as the effect of the application of PRP
Radice <i>et al</i> ^[38]	Comparative study (PRP vs control) 50 patients (25 vs 25)	ACL reconstructions with BPTB autograft (15 vs 10) or Hamstring (10 vs 15). Fixation in BPTB autograft with metallic interference screws, in hamstring autograft with metallic or bioabsorbable cross-pin in the femur and a bioabsorbable screw with a metallic staple in the proximal tibia PRP (produced with GPS III Kit, Biomet) was administered with the help of a sutured and compressed Gelfoam; 5 mL PRP was added homogeneously so as to completely cover the graft	ACL reconstruction with the use of PRPG achieved complete homogeneous grafts assessed by MRI, in 179 d compared with 369 d for ACL reconstruction without PRPG. This represented a time shortening of 48% with respect to ACL reconstruction without PRPG
Sánchez <i>et al</i> ^[39]	Comparative study (PRP vs control) 37 patients (22 vs 15)	ACL reconstruction with hamstring tendons, fixed with transcondylar screw proximally and PRGF-treated bone plug and two metal staples distally 6 mL PRP was produced with BTI System II (BTI Biotechnology Institute) and injected within the tendon graft fascicles with several punctures performed along the graft length, graft soaked in PRP until implantation and the remaining aliquots applied at the portals during suturing	PRGF resulted in more mature tissue than controls at histology ($P = 0.024$) Histologically evident newly formed connective tissue enveloping the graft was present in 77.3% of PRGF-treated grafts and 40% of controls Overall, arthroscopic evaluations were not statistically different between PRGF and control groups ($P = 0.051$)
Orrego <i>et al</i> ^[31]	Randomized trial (4 groups) 108 patients (27 control vs 26 PC vs 28 BP vs 27 PC + BP)	ACL reconstructions with quadruple semitendinosus-gracilis graft, fixed with a biodegradable transfixing pin proximally and a biodegradable interference screw distally; BP placed by interference fit at the femoral tunnel 5 mL PRP (produced with Biomet GPS II kit, Biomet) was added between the graft strands before passing it into the tunnel. After fixation, 1 mL of PRP was injected into the femoral tunnel between the graft strands	The use of PC had an enhancing effect on the graft maturation process evaluated only by MRI signal intensity at 6 mo follow-up
Ventura <i>et al</i> ^[27]	Randomized trial (PRP vs control) 20 patients (10 vs 10)	ACL reconstruction with quadruple hamstring tendon graft, with a femoral transcondylic fixation (BioTransFix, Arthrex) and tibial interference screw (BioRCL, Smith and Nephew) PRP was obtained according to the GPS Biomet-Merck technique (Biomet) and applied in femoral and tibial tunnels	CT highlighted a significant difference ($P < 0.01$) between ACL density of the two groups and showed that ACL density was similar to that of the posterior cruciate ligament in GF-treated group at 6 mo follow-up
- Figueroa <i>et al</i> ^[34]	Comparative study (PRP vs control) 50 patients (30 vs 20)	ACL reconstruction with hamstrings fixed with a femoral cross-pin and a tibial bio-absorbable interference screw PRP was produced with Magellan Magellan system (Medtronic, Minneapolis, MN) and applied under arthroscopy in both the tibial (3 mL) and femoral (3 mL) tunnels with a long needle syringe, and directly applied in the intra-articular graft portion (4 mL)	No statistically significant benefit in the PRP group in terms of graft maturation (ligamentization) at 6 mo of follow-up
Vogrin <i>et al</i> ^[33]	Randomized trial (PRP vs control) 41 patients (21 vs 20)	ACL reconstruction with double-looped semitendinosus and gracilis tendon graft fixed with two bioabsorbable cross pins in the femoral tunnel and one bioabsorbable interference screw in the tibial tunnel PRP was produced with Magellan system (Medtronic, Minneapolis, MN) and applied into the femoral and tibial tunnels as well as onto the graft itself	After 4-6 wk, significantly higher level of vascularization in the osteoligamentous interface in PRP group (0.33 ± 0.09 vs 0.16 ± 0.09 , $P < 0.001$). No evidence of revascularization in the intra-articular part in either group
ACL repair + Centeno <i>et al</i> ^[18]	Prospective study (BMC, PRP, PL) 10 patients	Pre-injection of hypertonic dextrose solution into the ACL using fluoroscopic guidance 2-5 d prior to BMC injection in order to prompt a brief inflammatory response in the ACL Intra-ligamentous injection of autologous BMC (harvested from iliac crest and isolated through	Patients included had ACL laxity on exam, and MRI evidence of grade 1, 2, or 3 ACL tears < 1 cm retraction 7/10 patients showed improvement in objective measures of ACL integrity in their post-procedure MRIs

		centrifugation), PRP and PL (prepared from venous blood <i>via</i> centrifugation and recentrifugation after freezing) using fluoroscopic guidance. Remaining BMCs were injected into the joint	The mean VAS change was a decrease of 1.7 ($P = 0.25$), the mean LEFS change was an increase of 23.3 ($P = 0.03$), and mean reported improvement was 86.7%
Seijas <i>et al</i> ^[19]	Retrospective study (PRGF-Endoret) 19 patients	PRGF-Endoret was produced using the technique described by Anitua and applied with a spine needle in both the proximal origin of the bundle and in the middle portion thereof in an amount of about 4 cc At the end of the surgery another injection of PRGF-Endoret was administered (6 cc) in the articular space.	16/19 professional soccer players with partial ACL tears returned to the same level Normal KT-1000 values in all operated cases Time to return to play: 16.2 ± 1.4 wk for Tegner 9 pts, 12.3 ± 1.1 for Tegner 10

PRP: Platelet rich plasma; ACL: Anterior cruciate ligament; PRFM: Platelet rich fibrin matrix; ACS: Autologous conditioned serum; PC: Platelet concentrate; BP: Bone plug; FT: Femoral tunnel; PLT: Posterolateral tunnel; AMT: Anteromedial tunnel; BPTB: Bone-patellar; PRGF: Plasma preparation rich in growth factors; BMC: Bone marrow concentrate; PL: Platelet lysate; VAS: Pain visual analog scale; NS: Non-significant; LEFS: Lower extremity functional scale.

enveloping by mature connective tissue, with signs of improved graft maturation, depending on the time passed from surgery.

DISCUSSION

The main findings of the present systematic review are that: (1) there is a paucity of clinical trials investigating the role of stem cells in promoting ACL healing, both in the treatment of partial and complete ACL tears. Therefore, no conclusive statement can be issued regarding the efficacy of this treatment approach; (2) despite the high number of RCTs, the role of PRP in ACL healing is still controversial, and it is not possible to fully endorse this biologic strategy to this particular indication; and (3) the use of biologic agents in partial ACL rupture is very limited, with just two clinical trials published, and therefore, the possibility of treating this kind of injuries by regenerative approaches remains an open question.

Biologic approaches to enhance healing of musculo-skeletal injuries are for sure a fashionable topic in the field of regenerative medicine. The overall brilliant results documented by *in vitro* and *in vivo* trials have stimulated their use in clinical practice, with different indications and targets, ranging from degenerative conditions (such as osteoarthritis and tendinopathies) to muscle and ligament injuries^[8,9]. The first product that has encountered a large clinical application (together with a large commercial success) is PRP, whose use has been documented in papers published more than a decade ago. Despite being no more a “novel” treatment option, there is still uncertainty about its real effectiveness and, up to the present moment, there is no clear recommendation for its use in any of the clinical conditions. Therefore, we underline the fact once again, that the positive findings from pre-clinical studies cannot be reproduced in the *in vivo* model, whose complexity cannot be fully mirrored in laboratory experiments^[40].

Looking at PRP potential in ACL healing, the literature is not conclusive with regards to the benefit of PRP application in providing a faster recovery and better functional outcome after ACL reconstruction. However, the evidence is currently limited to short term evaluations (up to 24 mo), whereas no trial has yet pointed out if the administration of platelet-derived growth factors could be effective at longer follow-up, providing more stable

results or lower rate of recurrent injury. Interestingly, most of the studies documented a superior graft maturation over time after PRP administration. These findings were achieved by imaging evaluation, and in one case also by histology^[39]. A better ligamentization of the graft may be related to superior and longer lasting mechanical properties that could impact clinical outcome at middle-to-long term evaluation. In light of that, further studies correlating imaging, histology and functional scores are expected to better clarify the role of PRP. Considering that patients after ACL reconstruction have high expectations in terms of durability of results, the possibility of reducing re-injury rate and providing a more stable clinical outcome seems very attractive and could justify the use of biologic agents. With regards to aspects such as bone-graft integration and prevention of bony tunnel enlargement, results are controversial and, overall, the majority of trials fail to support the use of PRP for this indication. By the way, research is moving forward in the attempt to optimize PRP technology to obtain the best possible results^[41]. The main limiting factor that scientists and clinicians have to overcome is the great inter-product variability and the absence of a well defined therapeutic protocol^[42]. When so many variables come into play, there is an intrinsic difficulty in finding the right way to move on. First of all, there are plenty of different PRP products that could be used. All of them differ in many fundamental aspects, such as preparation procedures, cellular content, platelet concentration rate, physical properties and eventual use of activators to enhance growth factors’ release. Authors have been using either lab made products or commercial kits from several companies, all characterized by different preparation protocols that rendered different PRP formulations^[11,43,44]. In particular, the aspect of cellularity is currently the most debated one and there are controversial findings regarding the role of the different components of PRP, especially leukocytes whose presence has been deemed as detrimental based on laboratory findings that have not been confirmed in the clinical setting, leaving many questions open to investigation^[45,46].

Another fundamental issue regards the application modalities of PRP during ACL reconstruction or repair. Several different approaches have been proposed, ranging from simple intra-articular injections to intra-ligamentary deposition, graft coating, topical use into

the bony tunnels, or at the bone-graft interface. Even more complex strategies, such as suturing PRP clots or PRP-soaked sponges directly onto the graft have been suggested. In any case, based on the available data, it is impossible to endorse an ideal product or an ideal therapeutic modality to stimulate ACL healing.

Looking at the application of mesenchymal stem cells, they have been introduced into clinical practice more recently than PRP, and they have been tested mainly in the field of cartilage regeneration/osteoarthritis^[47]. With regards to ACL healing, the current evidence is strongly affected by the paucity of literature available that prevents any indications for the use of such biological augmentation. As pointed out previously, only two papers in total (one RCT and one case series) investigated the potential efficacy of bone marrow concentrate in this particular field of sports medicine^[17,18]. One of these studies applied the stem cell concentrate to treat partial ACL tears together with PRP, which prevents any clear understanding of the real contribution of each biological product. The lack of data is a severe flaw, also considering that stem cell therapy is characterized by the same great variability described in the case of PRP products. Many factors should be taken into account. First of all, the source of stem cells should be considered, since it is possible to obtain them from different anatomical sites (bone marrow, adipose tissue, synovial tissue, peripheral blood and so on), and this peculiar aspect could play a major role in determining clinical outcome. Furthermore, stem cells could be used as a concentrate, or could be expanded *in vitro* and then applied during surgery^[48]. By the way, the application of cellular therapy in orthopaedics is under strict surveillance and clinicians have to face regulatory burdens that are currently limiting the number of ongoing clinical trials^[49]. For this reason, there is such a great dichotomy between the flourishing pre-clinical literature and the very limited data coming from clinical studies. This explains the fact that mainly bone marrow concentrate has been tested for ACL healing at the moment, since it is the easiest and safest way to collect and administer stem cells in a surgical setting. In light of these remarks, both in the field of PRP and stem cell augmentation for ACL healing, there is a need of further basic science studies to better understand the mechanisms of action of these powerful biological agents. Moreover, there is also a need of more high-level comparative trials that could clarify if some specific “products” or applicative modalities are truly better than others.

A further consideration should be issued on the ACL injury patterns that have been treated with biologic agents. The large majority of papers (21) were focused on their application during ACL reconstructive surgery, whereas only two trials, both case series, have investigated their potential in partial ACL tears (Table 1). The possibility of enhancing ACL healing in case of partial rupture is very attractive, because it can contribute to functional recovery and avoid the higher surgical stress of traditional reconstruction. However, even in this case,

the current lack of data prevents a reliable assessment of the efficacy of biologic agents, when applied for this specific purpose. The technique described in the literature to deliver PRP or stem cells into the injured ACL (intra-ligamentary injection under fluoroscopic or arthroscopic check) is feasible^[18,19] and results seem to be encouraging. Again further high quality trials, with higher number of patients and longer follow-up, are needed to confirm these preliminary findings. Furthermore, considering that partial ACL tears may have variable features, it would also be clinically relevant to introduce and validate a classification system, with the aim of understanding whether the biological approach could be more effective in specific lesion patterns.

In conclusion, based on the available clinical evidence, there is a lack of data about the efficacy of stem cells in ACL healing, whereas the data concerning the role of PRP are not conclusive to understand if it could provide a faster recovery and better functional outcome during ACL repair/reconstruction. Despite some positive findings in terms of graft maturation and clinical outcome, further long-term studies are needed to identify whether the administration of PRP could truly play a beneficial role during ACL reconstruction. Lastly, in contrast to the large number of trials dealing with ACL reconstruction, the treatment of partial ACL tears with biologic agents has been poorly investigated, and therefore there is need of more high quality data to understand the efficacy of biologic agents in this particular application.

COMMENTS

Background

Complete and partial anterior cruciate ligament (ACL) tears are among the most common injuries treated by orthopaedic surgeons every day. Currently, there are several surgical approaches that have been proposed to reconstruct/repair torn ACL and, despite overall satisfactory clinical outcome at medium-long term, there is still a failure rate up to 14% as documented by some studies. The current trend of research is aimed at finding solutions that could provide better and longer lasting results by stimulating ligament regeneration through the use of powerful biologic agents, such as platelet-rich plasma (PRP) and stem cells. The main goal is to achieve a tissue quality which is more similar to the one of the native ligament. The aim of the present paper is to systematically review the state of art regarding the application of biologic agents to promote ACL healing.

Research frontiers

Tissue engineering and regenerative approaches are currently widely applied in orthopaedics to stimulate healing of several tissues, from bone to cartilage and ligaments. In particular, PRP and stem cells are the most exploited strategies tested in clinical practice. Their application in the field of ACL healing (both for reconstruction and repair) represents the current cutting-edge technology to stimulate ligament regeneration in the attempt to improve clinical outcomes.

Innovations and breakthroughs

A total of 23 studies were included in the final analysis. In one paper stem cells were applied for ACL healing, in one paper there was a concomitant application of PRP and stem cells, whereas in the remaining 21 papers PRP was used. The main findings of the present systematic review are that: (1) there is a paucity of clinical trials investigating the role of stem cells in promoting ACL healing, both in the treatment of partial and complete ACL tears. Therefore, no conclusive indication can be issued regarding the efficacy of this treatment approach; (2) despite the high number of randomized controlled trials, the role of PRP in ACL healing is still controversial, and it is not possible to fully endorse this biologic

strategy to this particular indication; and (3) the use of biologic agents in partial ACL rupture is very limited, with only two clinical trials published, and therefore, the possibility of treating this kind of injuries by regenerative approaches remains an open question.

Applications

The application of PRP and stem cells in the field of ACL repair/reconstruction is technically feasible and safe. Several different approaches have been proposed, ranging from simple intra-articular injections to intra-ligamentary deposition, graft coating, topic use into the bony tunnels, or at the bone-graft interface. Even more complex strategies, such as suturing PRP-clots or PRP-soaked sponges directly onto the graft have been suggested. However, at present moment, it is impossible to endorse an ideal biologic product or an ideal therapeutic modality to stimulate ACL healing. There is a need of further basic studies to better understand the mechanisms of action of these powerful biological agents and also more high-level comparative trials are required to clarify if some specific "products" or applicative modalities are truly better than others.

Terminology

PRP is an autologous blood derivative which contains a higher concentration of platelets with respect to whole blood. The platelets act as a reservoir of a milieu of growth factors that could play a fundamental role in stimulating tissue healing and regeneration. Stem cells in orthopaedics are usually mesenchymal stem cells obtained from bone marrow. They can be concentrated or expanded in lab for being used as a biologic augmentation during surgical procedures or as an injective approach for treating a wide range of musculo-skeletal disorders.

Peer-review

This is a very interesting review article on biologic agents for ACL injury healing. It is well-written and has a correct methodology and structure.

REFERENCES

- 1 **Spindler KP**, Wright RW. Clinical practice. Anterior cruciate ligament tear. *N Engl J Med* 2008; **359**: 2135-2142 [PMID: 19005197 DOI: 10.1056/NEJMcip0804745]
- 2 **Prodromos CC**, Han Y, Rogowski J, Joyce B, Shi K. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen. *Arthroscopy* 2007; **23**: 1320-1325.e6 [PMID: 18063176 DOI: 10.1016/j.arthro.2007.07.003]
- 3 **Sonnery-Cottet B**, Colombet P. Partial tears of the anterior cruciate ligament. *Orthop Traumatol Surg Res* 2016; **102**: S59-S67 [PMID: 26797008 DOI: 10.1016/j.otsr.2015.06.032]
- 4 **Bollen S**. Epidemiology of knee injuries: diagnosis and triage. *Br J Sports Med* 2000; **34**: 227-228 [PMID: 10854030 DOI: 10.1136/bjsm.34.3.227-a]
- 5 **Järvelä T**. Double-bundle versus single-bundle anterior cruciate ligament reconstruction: a prospective, randomized clinical study. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 500-507 [PMID: 17216271 DOI: 10.1007/s00167-006-0254-z]
- 6 **Kongtharvonskul J**, Attia J, Thamakaisorn S, Kijkunasathian C, Woratanarat P, Thakkinstant A. Clinical outcomes of double- vs single-bundle anterior cruciate ligament reconstruction: a systematic review of randomized control trials. *Scand J Med Sci Sports* 2013; **23**: 1-14 [PMID: 22288837 DOI: 10.1111/j.1600-0838.2011.01439.x]
- 7 **Salmon L**, Russell V, Musgrove T, Pinczewski L, Refshauge K. Incidence and risk factors for graft rupture and contralateral rupture after anterior cruciate ligament reconstruction. *Arthroscopy* 2005; **21**: 948-957 [PMID: 16084292 DOI: 10.1016/j.arthro.2005.04.110]
- 8 **Filardo G**, Kon E, Roffi A, Di Matteo B, Merli ML, Marcacci M. Platelet-rich plasma: why intra-articular? A systematic review of preclinical studies and clinical evidence on PRP for joint degeneration. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2459-2474 [PMID: 24275957 DOI: 10.1007/s00167-013-2743-1]
- 9 **Di Matteo B**, Filardo G, Kon E, Marcacci M. Platelet-rich plasma: evidence for the treatment of patellar and Achilles tendinopathy—a systematic review. *Musculoskelet Surg* 2015; **99**: 1-9 [PMID: 25323041 DOI: 10.1007/s12306-014-0340-1]
- 10 **Boswell SG**, Cole BJ, Sundman EA, Karas V, Fortier LA. Platelet-rich plasma: a milieu of bioactive factors. *Arthroscopy* 2012; **28**: 429-439 [PMID: 22284405 DOI: 10.1016/j.arthro.2011.10.018]
- 11 **Dohan Ehrenfest DM**, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol* 2009; **27**: 158-167 [PMID: 19187989 DOI: 10.1016/j.tibtech.2008.11.009]
- 12 **Xie X**, Wu H, Zhao S, Xie G, Huangfu X, Zhao J. The effect of platelet-rich plasma on patterns of gene expression in a dog model of anterior cruciate ligament reconstruction. *J Surg Res* 2013; **180**: 80-88 [PMID: 23174707 DOI: 10.1016/j.jss.2012.10.036]
- 13 **Mastrangelo AN**, Vavken P, Fleming BC, Harrison SL, Murray MM. Reduced platelet concentration does not harm PRP effectiveness for ACL repair in a porcine in vivo model. *J Orthop Res* 2011; **29**: 1002-1007 [PMID: 21337615 DOI: 10.1002/jor.21375]
- 14 **Joshi SM**, Mastrangelo AN, Magarian EM, Fleming BC, Murray MM. Collagen-platelet composite enhances biomechanical and histologic healing of the porcine anterior cruciate ligament. *Am J Sports Med* 2009; **37**: 2401-2410 [PMID: 19940313 DOI: 10.1177/0363546509339915]
- 15 **Hao ZC**, Wang SZ, Zhang XJ, Lu J. Stem cell therapy: a promising biological strategy for tendon-bone healing after anterior cruciate ligament reconstruction. *Cell Prolif* 2016; **49**: 154-162 [PMID: 26929145 DOI: 10.1111/cpr.12242]
- 16 **Hirzinger C**, Tauber M, Korntner S, Quirchmayr M, Bauer HC, Traeweger A, Tempfer H. ACL injuries and stem cell therapy. *Arch Orthop Trauma Surg* 2014; **134**: 1573-1578 [PMID: 25073617 DOI: 10.1007/s00402-014-2060-2]
- 17 **Silva A**, Sampaio R, Fernandes R, Pinto E. Is there a role for adult non-cultivated bone marrow stem cells in ACL reconstruction? *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 66-71 [PMID: 23117168 DOI: 10.1007/s00167-012-2279-9]
- 18 **Centeno CJ**, Pitts J, Al-Sayegh H, Freeman MD. Anterior cruciate ligament tears treated with percutaneous injection of autologous bone marrow nucleated cells: a case series. *J Pain Res* 2015; **8**: 437-447 [PMID: 26261424 DOI: 10.2147/JPR.S86244]
- 19 **Seijas R**, Ares O, Cuscó X, Alvarez P, Steinbacher G, Cugat R. Partial anterior cruciate ligament tears treated with intraligamentary plasma rich in growth factors. *World J Orthop* 2014; **5**: 373-378 [PMID: 25035842 DOI: 10.5312/wjo.v5.i3.373]
- 20 **Magnussen RA**, Flanigan DC, Pedroza AD, Heinlein KA, Kaeding CC. Platelet rich plasma use in allograft ACL reconstructions: two-year clinical results of a MOON cohort study. *Knee* 2013; **20**: 277-280 [PMID: 23270598 DOI: 10.1016/j.knee.2012.12.001]
- 21 **Del Torto M**, Anea D, Panfoli N, Filardo G, Pace N, Chiusaroli M. Hamstrings anterior cruciate ligament reconstruction with and without platelet rich fibrin matrix. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3614-3622 [PMID: 25173508 DOI: 10.1007/s00167-014-3260-6]
- 22 **Darabos N**, Haspl M, Moser C, Darabos A, Bartolek D, Groenemeyer D. Intraarticular application of autologous conditioned serum (ACS) reduces bone tunnel widening after ACL reconstructive surgery in a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2011; **19** Suppl 1: S36-S46 [PMID: 21360125 DOI: 10.1007/s00167-011-1458-4]
- 23 **Vogrin A**, Ruppreht M, Crnjac A, Dinevski D, Krajnc Z, Recnik G. The effect of platelet-derived growth factors on knee stability after anterior cruciate ligament reconstruction: a prospective randomized clinical study. *Wien Klin Wochenschr* 2010; **122** Suppl 2: 91-95 [PMID: 20517680 DOI: 10.1007/s00508-010-1340-2]
- 24 **Valentí Azcárate A**, Lamo-Espinosa J, Aquerreta Beola JD, Hernandez Gonzalez M, Mora Gasque G, Valentí Nin JR. Comparison between two different platelet-rich plasma preparations and control applied during anterior cruciate ligament reconstruction. Is there any evidence to support their use? *Injury* 2014; **45** Suppl 4: S36-S41 [PMID: 25384473 DOI: 10.1016/S0020-1383(14)70008-7]
- 25 **Vadalá A**, Iorio R, De Carli A, Ferretti M, Paravani D, Caperna L, Iorio C, Gatti A, Ferretti A. Platelet-rich plasma: does it help reduce tunnel widening after ACL reconstruction? *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 824-829 [PMID: 22488012 DOI: 25323041 DOI: 10.1007/s12306-014-0340-1]

- 10.1007/s00167-012-1980-z]
- 26 **Nin JR**, Gasque GM, Azcárate AV, Beola JD, Gonzalez MH. Has platelet-rich plasma any role in anterior cruciate ligament allograft healing? *Arthroscopy* 2009; **25**: 1206-1213 [PMID: 19896041 DOI: 10.1016/j.arthro.2009.06.002]
 - 27 **Ventura A**, Terzaghi C, Borgo E, Verdoia C, Gallazzi M, Failoni S. Use of growth factors in ACL surgery: Preliminary study. *J Orthopaed Traumatol* 2005; **6**: 76-79 [DOI: 10.1007/s10195-005-0085-6]
 - 28 **Starantzis KA**, Mastrokalos D, Koulalis D, Papakonstantinou O, Soucacos PN, Papagelopoulos PJ. The Potentially Positive Role of PRPs in Preventing Femoral Tunnel Widening in ACL Reconstruction Surgery Using Hamstrings: A Clinical Study in 51 Patients. *J Sports Med (Hindawi Publ Corp)* 2014; **2014**: 789317 [PMID: 26464895 DOI: 10.1155/2014/789317]
 - 29 **Mirzatooleei F**, Alamdari MT, Khalkhali HR. The impact of platelet-rich plasma on the prevention of tunnel widening in anterior cruciate ligament reconstruction using quadrupled autologous hamstring tendon: a randomised clinical trial. *Bone Joint J* 2013; **95-B**: 65-69 [PMID: 23307675 DOI: 10.1302/0301-620X.95B1.30487]
 - 30 **Silva A**, Sampaio R, Pinto E. Femoral tunnel enlargement after anatomic ACL reconstruction: a biological problem? *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1189-1194 [PMID: 20111952 DOI: 10.1007/s00167-010-1046-z]
 - 31 **Orrego M**, Larrain C, Rosales J, Valenzuela L, Matas J, Durruty J, Sudy H, Mardones R. Effects of platelet concentrate and a bone plug on the healing of hamstring tendons in a bone tunnel. *Arthroscopy* 2008; **24**: 1373-1380 [PMID: 19038708 DOI: 10.1016/j.arthro.2008.07.016]
 - 32 **Ruprecht M**, Vogrin M, Hussein M. MRI evaluation of tibial tunnel wall cortical bone formation after platelet-rich plasma applied during anterior cruciate ligament reconstruction. *Radiol Oncol* 2013; **47**: 119-124 [PMID: 23801907 DOI: 10.2478/raon-2013-0009]
 - 33 **Vogrin M**, Ruprecht M, Dinevski D, Hašpl M, Kuhta M, Jevsek M, Knežević M, Rožman P. Effects of a platelet gel on early graft revascularization after anterior cruciate ligament reconstruction: a prospective, randomized, double-blind, clinical trial. *Eur Surg Res* 2010; **45**: 77-85 [PMID: 20814217 DOI: 10.1159/000318597]
 - 34 **Figueroa D**, Melean P, Calvo R, Vaisman A, Zilleruelo N, Figueroa F, Villalón I. Magnetic resonance imaging evaluation of the integration and maturation of semitendinosus-gracilis graft in anterior cruciate ligament reconstruction using autologous platelet concentrate. *Arthroscopy* 2010; **26**: 1318-1325 [PMID: 20800986 DOI: 10.1016/j.arthro.2010.02.010]
 - 35 **Silva A**, Sampaio R. Anatomic ACL reconstruction: does the platelet-rich plasma accelerate tendon healing? *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 676-682 [PMID: 19288080 DOI: 10.1007/s00167-009-0762-8]
 - 36 **Seijas R**, Ares O, Catala J, Alvarez-Diaz P, Cusco X, Cugat R. Magnetic resonance imaging evaluation of patellar tendon graft remodelling after anterior cruciate ligament reconstruction with or without platelet-rich plasma. *J Orthop Surg (Hong Kong)* 2013; **21**: 10-14 [PMID: 23629979]
 - 37 **Ruprecht M**, Jevtić V, Serša I, Vogrin M, Jevšek M. Evaluation of the tibial tunnel after intraoperatively administered platelet-rich plasma gel during anterior cruciate ligament reconstruction using diffusion weighted and dynamic contrast-enhanced MRI. *J Magn Reson Imaging* 2013; **37**: 928-935 [PMID: 23097413 DOI: 10.1002/jmri.23886]
 - 38 **Radice F**, Yáñez R, Gutiérrez V, Rosales J, Pinedo M, Coda S. Comparison of magnetic resonance imaging findings in anterior cruciate ligament grafts with and without autologous platelet-derived growth factors. *Arthroscopy* 2010; **26**: 50-57 [PMID: 20117627 DOI: 10.1016/j.arthro.2009.06.030]
 - 39 **Sánchez M**, Anitua E, Azofra J, Prado R, Muruzabal F, Andia I. Ligamentization of tendon grafts treated with an endogenous preparation rich in growth factors: gross morphology and histology. *Arthroscopy* 2010; **26**: 470-480 [PMID: 20362825 DOI: 10.1016/j.arthro.2009.08.019]
 - 40 **Di Matteo B**, Kon E, Filardo G. Intra-articular platelet-rich plasma for the treatment of osteoarthritis. *Ann Transl Med* 2016; **4**: 63 [PMID: 26904585 DOI: 10.3978/j.issn.2305-5839.2016.01.18]
 - 41 **Kon E**, Filardo G, Di Matteo B, Marcacci M. PRP for the treatment of cartilage pathology. *Open Orthop J* 2013; **7**: 120-128 [PMID: 23730375 DOI: 10.2174/1874325001307010120]
 - 42 **Tschon M**, Fini M, Giardino R, Filardo G, Dallari D, Torricelli P, Martini L, Giavaresi G, Kon E, Maltarello MC, Nicolini A, Carpi A. Lights and shadows concerning platelet products for musculoskeletal regeneration. *Front Biosci (Elite Ed)* 2011; **3**: 96-107 [PMID: 21196289 DOI: 10.2741/e224]
 - 43 **Mautner K**, Malanga GA, Smith J, Shiple B, Ibrahim V, Sampson S, Bowen JE. A call for a standard classification system for future biologic research: the rationale for new PRP nomenclature. *PM R* 2015; **7**: S53-S59 [PMID: 25864661 DOI: 10.1016/j.pmrj.2015.02.005]
 - 44 **Loibl M**, Lang S, Brockhoff G, Gueorguiev B, Hilber F, Worlicek M, Baumann F, Grechenig S, Zellner J, Huber M, Valderrabano V, Angele P, Nerlich M, Prantl L, Gehmert S. The effect of leukocyte-reduced platelet-rich plasma on the proliferation of autologous adipose-tissue derived mesenchymal stem cells. *Clin Hemorheol Microcirc* 2016; **61**: 599-614 [PMID: 25536920 DOI: 10.3233/CH-141920]
 - 45 **Assirelli E**, Filardo G, Mariani E, Kon E, Roffi A, Vaccaro F, Marcacci M, Facchini A, Pulsatelli L. Effect of two different preparations of platelet-rich plasma on synoviocytes. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2690-2703 [PMID: 24942296 DOI: 10.1007/s00167-014-3113-3]
 - 46 **Kreuz PC**, Krüger JP, Metzclaff S, Freymann U, Endres M, Pruss A, Petersen W, Kaps C. Platelet-Rich Plasma Preparation Types Show Impact on Chondrogenic Differentiation, Migration, and Proliferation of Human Subchondral Mesenchymal Progenitor Cells. *Arthroscopy* 2015; **31**: 1951-1961 [PMID: 25980401 DOI: 10.1016/j.arthro.2015.03.033]
 - 47 **Mamidi MK**, Das AK, Zakaria Z, Bhonde R. Mesenchymal stromal cells for cartilage repair in osteoarthritis. *Osteoarthritis Cartilage* 2016; **24**: 1307-1316 [PMID: 26973328 DOI: 10.1016/j.joca.2016.03.003]
 - 48 **Caplan AI**. Review: mesenchymal stem cells: cell-based reconstructive therapy in orthopedics. *Tissue Eng* 2005; **11**: 1198-1211 [PMID: 16144456 DOI: 10.1089/ten.2005.11.1198]
 - 49 **Chirba MA**, Sweetapple B, Hannon CP, Anderson JA. FDA regulation of adult stem cell therapies as used in sports medicine. *J Knee Surg* 2015; **28**: 55-62 [PMID: 25603042 DOI: 10.1055/s-0034-1398470]

P- Reviewer: Bicanic G, Hernandez-Sanchez S, Kulshrestha V
S- Editor: Gong XM **L- Editor:** Wang TQ **E- Editor:** Li D



Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik, Department of Sports Medicine and Orthopaedic Surgery, Máxima Medical Center, 5600PD, Eindhoven, The Netherlands

Rob Paulus Augustinus Janssen, Max Reijman, Daan Martijn Janssen, Jan Bernardus Antonius van Mourik, Department of Orthopaedics and Trauma, Máxima Medical Center, 5500 Veldhoven, The Netherlands

Max Reijman, Department of Orthopaedic Surgery Erasmus MC, University Medical Center Rotterdam, 3100 Rotterdam, The Netherlands

Author contributions: Janssen RPA, Janssen DM, Reijman M and van Mourik JBA performed the systematic review; Reijman M performed the statistical analysis; Janssen RPA and Reijman M wrote the paper.

Conflict-of-interest statement: None of the authors have any conflict of interest in this research.

Data sharing statement: No data were created so no data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Rob Paulus Augustinus Janssen, MD, PhD, Department of Sports Medicine and Orthopaedic Surgery, Máxima Medical Center, Postbus 90052, 5600PD, Eindhoven, The Netherlands. r.janssen@mmc.nl
Telephone: +31-40-8885936
Fax: +31-40-8885938

Received: February 17, 2016
Peer-review started: February 19, 2016
First decision: March 25, 2016
Revised: May 14, 2016
Accepted: June 1, 2016
Article in press: June 3, 2016
Published online: September 18, 2016

Abstract

AIM

To summarize the current knowledge on vascular complications and deep venous thrombosis (DVT) prophylaxis after anterior cruciate ligament (ACL) reconstruction.

METHODS

A systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement. MEDLINE, EMBASE, Cochrane, Web of Science, CINAHL, PubMed publisher, and Google scholar medical literature databases were searched up to November 10, 2015. Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction of all graft types in humans was included. A risk of bias assessment was determined.

RESULTS

Forty-seven studies were included in the review. Pseudaneurysms were the most frequently reported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation with an incidence of 0.3%. The time to diagnosis of arterial complications after ACL reconstruction varied from days to mostly weeks but even years. After ACL reconstruction without thromboprophylaxis, the incidence of DVT was 9.7%, of which 2.1% was symptomatic. The incidence of pulmonary embolism was 0.1%. Tourniquet time

> 2 h was related to venous thromboembolism. Thromboprophylaxis is indicated in patients with risk factors for venous thromboembolism.

CONCLUSION

After ACL reconstruction, the incidence of arterial complications, symptomatic DVT and pulmonary embolism was 0.3%, 2.1% and 0.1% respectively. Arterial complications may occur with all types of arthroscopic ACL reconstruction, methods of graft fixation as well as any type of graft. Patients considered to be at moderate or high risk of venous thromboembolism should routinely receive thromboprophylaxis after ACL reconstruction.

Key words: Anterior cruciate ligament reconstruction; Arterial complication; Pseudoaneurysm; Venous thromboembolism; Pulmonary embolism; Thromboprophylaxis

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Vascular complications after anterior cruciate ligament (ACL) reconstruction of the knee may present serious morbidity and even mortality. Although rare, it is necessary to understand the main risks and symptoms of these devastating lesions. This systematic review presents the current knowledge on arterial injuries, venous thromboembolism and thromboprophylaxis after ACL reconstruction.

Janssen RPA, Reijman M, Janssen DM, van Mourik JBA. Arterial complications, venous thromboembolism and deep venous thrombosis prophylaxis after anterior cruciate ligament reconstruction: A systematic review. *World J Orthop* 2016; 7(9): 604-617 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/604.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.604>

INTRODUCTION

Vascular complications after anterior cruciate ligament (ACL) reconstructions cause serious morbidity and potential mortality^[1]. They can be categorized in arterial and venous thromboembolic complications. The incidence of arterial complications after ACL reconstruction is unknown^[1]. Case reports have been published using various techniques of ACL reconstruction^[1].

Venous thromboembolism (VTE) after ACL reconstruction may present clinically as symptomatic or asymptomatic deep venous thrombosis (DVT), pulmonary embolism (PE) and postthrombotic syndrome^[1-3]. The incidence of VTE after ACL reconstruction varies from 0.2%-14%^[1,2,4-11]. The variable incidence of VTE after ACL reconstruction depends on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography), the heterogeneity of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and

postoperative mobilisation) and DVT prophylaxis^[1,12]. Deep venous thrombosis may cause pulmonary embolism which may be fatal in its immediate course or may result in pulmonary hypertension in the long term^[1,13]. The postthrombotic syndrome may cause serious morbidity and affects 23% of limbs 2 years after DVT, 35%-69% and 49%-100% at 3 and at 5-10 years respectively^[1,4,14]. ACL reconstruction ranks number 6 of most performed orthopedic operations^[15]. However uniform evidence-based clinical practice guidelines for DVT prophylaxis after ACL reconstruction are lacking^[1,2,16].

A thorough understanding of the incidence, risk factors and potential methods for prevention of vascular complications after ACL reconstruction is critical to optimize patient safety^[17]. This systematic review presents the current knowledge of arterial complications, VTE and thromboprophylaxis after arthroscopic ACL reconstruction. The review will highlight the incidence, types and risk factors of arterial complications and VTE after ACL reconstruction as well as the current recommendations for DVT prophylaxis.

MATERIALS AND METHODS

The reporting in this systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement^[18].

Eligibility criteria

Inclusion criteria were all study designs evaluating arterial complications and VTE after ACL reconstruction. Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction of all graft types was included. Only human *in vivo* studies were eligible for inclusion in the systematic review. The full inclusion and exclusion criteria are presented in Table 1.

Electronic search

MEDLINE, EMBASE, Cochrane, Web of Science, CINAHL, PubMed publisher, and Google scholar medical literature databases were searched up to November 10, 2015. Search terms included synonyms for anterior cruciate ligament reconstruction, and synonyms for vascular complications. Additionally, the reference lists of all eligible studies were manually screened.

Study selection

All eligible articles were screened by title and abstract by 2 teams of reviewers. One author screened all abstracts and 2 co-authors scored both half of the abstracts independently of the first author. After this first inclusion, the full-text articles were assessed. Disagreements on inclusions were resolved by discussion and, if necessary, a final decision was made by a fourth reviewer. Furthermore, all references of both excluded and included articles were analyzed for eligible articles. The consequences of the search strategy (screening

Table 1 Inclusion and exclusion criteria

<p>Inclusion criteria</p> <p>Studies (randomized, non-randomized, case series, prospective or retrospective design, case reports) evaluating vascular and thromboembolic complications after ACL reconstruction</p> <p>All types of ACL reconstruction surgery related arterial and venous complications</p> <p>All types of ACL reconstruction surgery related thromboembolic complications</p> <p>Any arthroscopic surgical method of primary or revision intra-articular ACL reconstruction</p> <p>All graft types for ACL reconstruction</p> <p>Multiligament reconstructions including ACL</p> <p>Combined ACL reconstruction and meniscal surgery</p> <p>Human <i>in vivo</i> studies with reported outcome</p> <p>English language</p> <p>Full text available</p> <p>Exclusion criteria</p> <p>Animal studies</p> <p>Cadaveric studies</p> <p>Nonsurgical related vascular or thromboembolic complications</p>

ACL: Anterior cruciate ligament.

of title and abstract) are that only those studies will be eligible for inclusion if arterial complications, VTE or DVT prophylaxis after ACL reconstruction are reported in the abstracts. Studies that did not report these findings in their abstract were consequently not included in the current review.

Data collection process

Two reviewers extracted the study characteristics, type of vascular complications, and if available the incidence of vascular complications in the study population.

Data items

The data included study type, patient demographics, type and incidence of vascular or thromboembolic complication (arterial, pulmonary embolism, symptomatic or asymptomatic DVT), surgical technique, graft type, graft fixation method, thromboprophylaxis, tourniquet time and pressure and comorbidity for vascular and thromboembolic complications.

Synthesis of results

Incidence of DVT (separated for all and symptomatic) and PE was pooled of the studies reporting data of isolated ACL reconstruction without thromboprophylaxis. Additionally, the incidence numbers of those studies with low risk of bias on the items patient selection and classification were pooled.

Assessment of risk of bias

Risk of bias was assessed in the studies used for the determination of the incidence of vascular and/or venous complications following an ACL reconstruction procedure. Risk of bias was not assessed for case reports. Two reviewers independently assessed the risk of bias of the studies. In case of disagreement, the

two reviewers tried to achieve consensus. If consensus was not achieved, a third reviewer was asked for final judgment. Those items of the checklist of the Dutch Cochrane Centre of risk of bias of studies reporting the incidence of adverse events, suitable for the current study objectives, were used for the risk of bias assessment^[19]. All items could be rated "positive" (+), "negative" (-) or "not clear" (?).

Studies were classified as low risk of selection bias when they scored "positive" on the item: "The authors reported inclusion of 'all' or 'consecutive' patients". Studies were classified as low risk of information bias when they scored "positive" on the items: "Follow-up period was minimally 1 year" and "if all included patients were evaluated for complications".

Research questions

The following research questions were formulated.

Arterial complications: (1) What is the incidence of arterial complications after ACL reconstruction? (2) What types of arterial complications occur after ACL reconstruction? (3) Is there a correlation between arterial complications and fixation methods for ACL reconstruction? (4) What is the time to diagnosis of arterial complications after ACL reconstruction?

Venous complications: (1) What is the incidence of VTE after ACL reconstruction without thromboprophylaxis? (2) Is tourniquet time related to VTE after ACL reconstruction? (3) Is thromboprophylaxis indicated after ACL reconstruction?

RESULTS

Study selection

The PRISMA flow chart of the systematic review is presented in Figure 1. A total of 47 studies were included: 2 randomized controlled trials (RCT)^[20,21], 8 prospective cohort studies^[5,6,10,11,22-25], 9 retrospective cohort studies^[2,4,7,8,26-30] and 28 case reports^[13,31-57].

Risk of bias assessment

The results of the risk of bias assessment for the included studies are presented in Table 2. Case reports were not eligible for risk of bias assessment.

Details of arterial complications and thromboprophylaxis

The results of the arterial complications are specified in Table 3. The details of VTE and thromboprophylaxis are detailed in Table 4. Table 5 presents the incidence of DVT and PE after pooling the data for isolated ACL reconstructions without thromboprophylaxis.

Results of individual studies and answers to research questions

Arterial complications: (1) What is the incidence of arterial complications after ACL reconstruction?

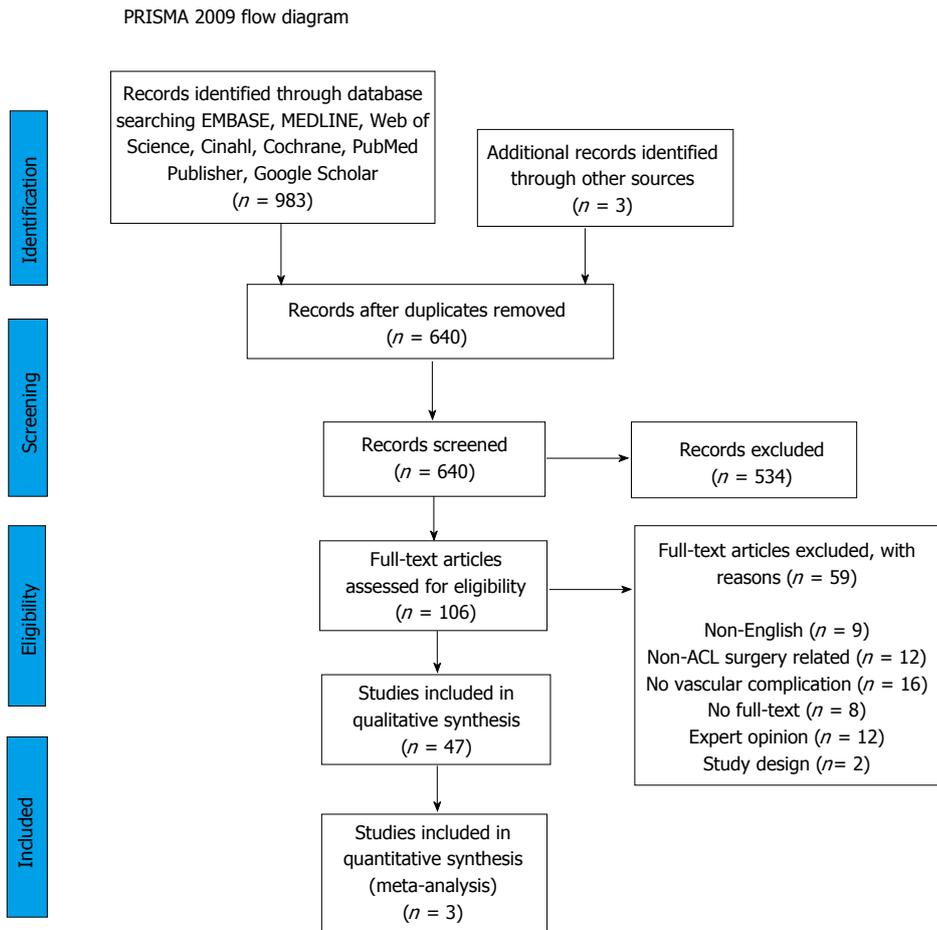


Figure 1 Prisma flow chart. ACL: Anterior cruciate ligament.

Table 2 Risk of bias of studies reporting venous complications

Ref.	Study design	Patient selection ¹	Follow-up ²	Classification ³
Adala <i>et al</i> ^[6]	PC	+	-	+
Born <i>et al</i> ^[26]	RS	+	-	-
Cullison <i>et al</i> ^[10]	PC	?	-	+
Dong <i>et al</i> ^[8]	RS	?	-	+
Ettema <i>et al</i> ^[27]	RS	-	?	-
Gaskill <i>et al</i> ^[2]	RS	+	-	-
Hetsroni <i>et al</i> ^[30]	RS	?	?	-
Hirota <i>et al</i> ^[22]	PC	-	-	+
Hirota <i>et al</i> ^[25]	PC	-	-	+
Jameson <i>et al</i> ^[28]	RS	?	-	-
Jaureguito <i>et al</i> ^[7]	RS	+	-	+
Lind <i>et al</i> ^[23]	PC	+	?	-
Maletis <i>et al</i> ^[11]	PC	?	?	-
Marlovits <i>et al</i> ^[20]	RCT	-	-	+
Mohtadi <i>et al</i> ^[21]	RCT	+	+	-
Struijk-Mulder <i>et al</i> ^[5]	PC	+	-	+
Sun <i>et al</i> ^[29]	RS	+	-	+
Williams <i>et al</i> ^[24]	PC	-	-	+
Ye <i>et al</i> ^[4]	RS	?	-	+

¹Inclusion of consecutive patients; ²Was follow-up period adequate (minimum 1 year) for exposure of adverse event? ³Was the used classification shown to be valid and reliable? +: Yes; -: No; ?: Not clear; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study.

Twenty-two studies reported arterial complications after ACL reconstruction. These papers described a total of 23 case reports. Arterial complications after ACL reconstruction are rare. The incidence of arterial lesions after ACL reconstruction is only described in 1 study. Janssen *et al*^[45] have analysed their consecutive series retrospectively and found an incidence of 0.3% for arterial pseudoaneurysm in a series of 299 arthroscopic ACL reconstructions.

The incidence of arterial complications after ACL reconstruction is very low. The incidence of 0.3% presented in a retrospective series may be overestimated considering the fact that only case reports have been published in the literature. Long-term studies are necessary for analysis of the incidence of arterial complications after ACL reconstruction.

(2) What types of arterial complications occur after ACL reconstruction? Table 3 presents the details of the 23 published arterial complications after ACL reconstruction. The described complications were arterial-occlusions, avulsions, penetrating injuries, arteriovenous fistulae or pseudoaneurysms. Pseudoaneurysm was the most frequently reported arterial complication (13 cases). Various arteries around the knee were injured: Popliteal artery, posterior tibial

Table 3 Results arterial injuries (case reports)

Ref.	ACLR	Graft type	Fixation femur	Fixation tibia	Vascular injury	Diagnosis after ACLR	Treatment	Cause vascular complication
Spalding <i>et al</i> ^[31]	Primary	Gore-Tex	?	?	Compression popliteal artery	8 yr	Cyst removal	Compression by cyst containing ruptured Gore-tex graft
Aldridge <i>et al</i> ^[32]	Primary	BPTB	Interference screw	Interference screw	Avulsion middle gen. artery	4 wk	Direct repair avulsion	Lesion artery by shaver
Evans <i>et al</i> ^[33]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	5 wk	Ligation pseudoaneurysm	Elevation periosteum medial tibia (tunnel preparation)
Friederich <i>et al</i> ^[34]	Primary	BPTB	Staples	Staples	Lesion sup. lat. gen. artery	5 mo	Removal staples	Hardware femur
Kanko <i>et al</i> ^[35]	Primary	BPTB	Interference screw	Bicortical screw	Pseudoaneurysm popliteal artery	2 yr	Ligation pseudoaneurysm	Drill bit for bicortical tibia fixation?
Keçeci <i>et al</i> ^[36]	Primary	BPTB	Interference screw	Interference screw	Popliteal arteriovenous fistula	18 mo	Venous re-anastomosis	Break-out posterior femoral cortex
Lamo-Espinosa <i>et al</i> ^[37]	Primary	BPTB	Interference screw	Interference screw	Lesion lat. inf. gen. artery	1 d	Embolization	Simultaneous lateral meniscectomy
Mello <i>et al</i> ^[38]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	6 wk	Embolization	Direct lesion artery by shaver
Pereira <i>et al</i> ^[39]	Primary	BPTB	Interference screw	Interference screw	Pseudoaneurysm sup. lat. gen. artery	11 d	Ligation pseudoaneurysm	Hardware femur
Roth <i>et al</i> ^[40]	Primary	BTPB + augmentation	Staple	?	Occlusion popliteal artery	6 wk	Venous bypass	Entrapment between graft and femur
Tam Kelvin <i>et al</i> ^[41]	Primary	BPTB	Endobutton	Interference screw	Pseudoaneurysm popliteal artery	8 d	Repair by venous graft	Direct trauma by guide pin femoral canal
Lee <i>et al</i> ^[42]	Rerevision	?	Rigidfix cross pin	?	2 lesions sup. to level of med. and lat. gen. artery	6 wk	Venous re-anastomosis	Drill tip for Rigidfix cross pin
Ambrosia <i>et al</i> ^[57]	Primary	Hamstring	TightRope	Interference screw	Pseudoaneurysm popliteal artery	7 wk	Venous bypass	Hamstring harvest/previous catheterization-angioplasty?
Buda <i>et al</i> ^[43]	Primary	Hamstring ACL + allograft PCL	Staples	Staples	Pseudoaneurysm post. tibial artery	1 wk	Embolization	Surgical approach PCL or hamstring harvest?
Galanakis <i>et al</i> ^[44]	Primary	Hamstring + extra-artic. rec.	Staples	Pes anserinus	Pseudoaneurysm popliteal artery	Day of surgery	Venous re-anastomosis	Lesion artery by shaver and popliteal entrapment syndrome
Janssen <i>et al</i> ^[45]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Pseudoaneurysm popliteal artery	12 d	Venous repair	Drill tip for bicortical tibial fixation
Janssen <i>et al</i> ^[47]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Subtotal occlusion popliteal artery	19 d	Embolectomy	Preexistent intimal lesion after knee dislocation
Janssen <i>et al</i> ^[47]	Primary	Hamstring	Bone Mulch Screw	WasherLoc	Pseudoaneurysm and occlusion popliteal artery	9 d	Venous re-anastomosis	Drill tip for bicortical tibial fixation
Milankov <i>et al</i> ^[48]	Primary	Hamstring	Interference screw	Interference screw	Pseudoaneurysm med. inf. gen. artery	1 d	Ligation pseudoaneurysm	Hamstring harvest?
Panigrahi <i>et al</i> ^[56]	Primary	Hamstring ACL + PCL	?	?	Occlusion popliteal artery	Day of surgery	Embolectomy	Preexistent thrombotic occlusion after knee dislocation
Tsubosaka <i>et al</i> ^[54]	Primary	Hamstring	Cortical buttons	Screw post	Pseudoaneurysm med. inf. gen. artery	2 d	Embolization	Anteromedial portal
Pereira <i>et al</i> ^[39]	Revision	Hamstring	Transverse screw	Interference screw	Pseudoaneurysm sup. lat. gen. artery	2 d	Ligation pseudoaneurysm	Hardware femur
Carr <i>et al</i> ^[49]	Primary	Achilles tendon allograft	Interference screw	Suture+ washer bone plug	Traumatic arteriovenous fistula	7 wk	Ligation fistula	Injury at medial superior portal site

ACL: Anterior cruciate ligament; ACLR: ACL reconstruction; BPTB: Bone-patellar tendon-bone; PCL: Posterior cruciate ligament.

Table 4 Data venous thromboembolism and thromboprophylaxis

Ref.	Study design	Number ACLR	Mean age (yr)	Male (M) Female (F)	Graft type	Mean duration surgery (min)	Mean tourniquet time (min)	BMI (kg/m ²)	Thromboprophylaxis	Hospital stay (d)
Marlovits <i>et al</i> ^[20]	RCT	140 (87 vs 88 placebo)	29.9 ± 7.4 vs 30.2 ± 6.9	M 63% F 60%	BTPB	Mean > 120	?	Comparable between groups	Yes (enoxaparin 3-8 d + 20 d enoxaparin vs enoxaparin 3-8 d + placebo)	3-8
Mohtadi <i>et al</i> ^[21]	RCT	330	28.5 (14-50)	M 183 F 147	BPTB, hamstring	?	?	?	?	?
Adala <i>et al</i> ^[6]	PC	112	31.6	M 61 F 51	Hamstring	64.9 ± 7.8	?	?	None	2
Cullison <i>et al</i> ^[10]	PC	67	26.5 (19-39)	All men	BPTB	?	83 (0-115)	?	None	?
Hirota <i>et al</i> ^[25]	PC	30	24.1 ± 8.3	M 14 F 16	?	?	?	?	None	?
Hirota <i>et al</i> ^[22]	PC	40 (20 ACLR vs 20 TKA)	26.7 ± 13.4 vs 71.3 ± 6.8	M:F ACLR 10:10 vs TKA 6:14	?		87.1 ± 24.4 vs 87.2 ± 18.4	?	None	?
Lind <i>et al</i> ^[23]	PC	5818	?	M approximately 57%	BPTB and hamstring	Prim. ACLR 69.4 ± 21.1; rev. ACLR 90.0 ± 32.3	?	?	18.5% (prim. ACLR 15.7%; rev. ACLR 20.8%)	?
Maletis <i>et al</i> ^[11]	PC	Prim. ACLR 15101	Prim. ACLR 29.5 ± 11.5	M 9604 F 5497	Autograft 57.6%, allografts 42.4%	?	?	≥ 30 = 23.3%	?	?
		Rev. ACLR 1091	Rev. ACLR 29.8 ± 10.7	M 693 F 398	Autograft 20.9%, allografts 78.8%	?	?	≥ 30 = 20.8%	?	?
Struijk-Mulder <i>et al</i> ^[5]	PC	100	30.0 ± 10.0	M 77 F 23	Autograft HS 84, BPTB 14 allograft 2	68.0 ± 22.0	76.0 ± 23.0	25.0 ± 4.0	None	1 to 2
Williams <i>et al</i> ^[24]	PC	23	31 (19-42)	M 17 F 6	BPTB	?	103 (89-136)	?	None	2-3
Born <i>et al</i> ^[26]	RC	136 ACLR + multiligament rec.	VTE group 42 (24-43); Non-VTE group 31 (SD 11)	DVT group M: F 3:0; Non-VTE group 103:28	?	VTE group 152.0; Non-VTE group 233 ± 76	VIE group 78.0; Non-VIE group 102 ± 54	VTE group 35 (28-42); Non-VTE group 30 (SD 7)	Yes (before 2007, 3 wk aspirin. After 2007, LMWH 3 wk)	?
Dong <i>et al</i> ^[8]	RC	152 ACLR	34.9	M 91 F 61	Hamstring/allograft	?	3 groups < 90, 90-120, > 120	22.6	None	?
Ettema <i>et al</i> ^[27]	RC	?	?	?	?	?	?	?	50% prescribed LMWH or coumarin during hospital stay; 5% for 1-2 wk; 2% for 3-4 wk and 35% for 6 wk	?
Gaskill <i>et al</i> ^[2]	RC	15767 ACLR + HTO/PCL non specified	28.9 (SD 7.6)	M 13794	?	?	?	27.8	?	?
Hetsroni <i>et al</i> ^[30]	RC	58863 ACLR, total 418323 arthroscopies	PE group 50.3 (15-79) vs non-PE group 45.5 (0-100)	F 2764 PE group F 57.3% vs non-PE group F 46.8%	?	?	?	(SD 4.0) ?	?	?
Jameson <i>et al</i> ^[28]	RC	13941	29.3 (8-83)	F 46.8% M 79.5%	?	?	?	?	?	1-4

Jaureguito <i>et al</i> ^[7]	RC	131 group 1 (knee arthroscopy)	?	F 20.5% M 73	-	?	?	?	Aspirin (325 mg) daily for 3 wk postsurgery if age > 45 yr Idem	?
		108 group 2 (ACL, osteotomy)		F 58 M 60	?	?	?	?		?
Sun <i>et al</i> ^[29]	RC	231	23.6	F 48 M 69.3%	?	88.4	67.5	24.5	None	?
Ye <i>et al</i> ^[4]	RC	171	30.1 ± 10.0	F 30.7% M 123 F 48	Hamstring	86.9 ± 26.4	69.9 ± 15.9	24.4 ± 3.2	None	4
Ackerman <i>et al</i> ^[55]	CR	1	45	F 1	BPTB	?	0	?	Aspirin 325 mg daily none	Outpatient
Chien <i>et al</i> ^[50]	CR	1	34	M 1	?	110	?	30	LMWH during hospital stay	?
Janssen <i>et al</i> ^[13]	CR	1	19	F 1	Hamstring	96	110	27.5	None	3
Kang <i>et al</i> ^[51]	CR	1 (+MCL rec.)	48	F 1	Hamstring	?	90	?	None	?
Liu <i>et al</i> ^[52]	CR	1	34	M 1	Hamstring	110	119	30.1	None	5
Theron <i>et al</i> ^[53]	CR	1	30	F 1	?	?	?	?	?	Occurred day after surgery

ACL: ACL reconstruction; BPTB: Bone-patellar tendon-bone; TKA: Total knee arthroplasty; LMWH: Low molecular weight heparin; HTO: High tibial osteotomy; VTE: Venous thromboembolism; PCL: Posterior cruciate ligament; prim: Primary; MCL: Medial collateral ligament; rev: Revision; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study; CR: Case report; SD: Standard deviation; DVT: Deep venous thrombosis; rec.: Reconstruction.

artery, medial and lateral inferior genicular arteries and lateral superior genicular artery. Clinical presentations were repeated hemarthrosis, pain and a pulsatile mass after ACL reconstruction.

The types of arterial complications after ACL reconstruction may be categorized in arterial- occlusions, avulsions, penetrating injuries, arteriovenous fistulae or pseudoaneurysms. Pseudoaneurysm is the most common arterial complication (13/23 cases).

(3) Is there a correlation between arterial complications and fixation methods for ACL reconstruction? Twenty-three case reports on arterial complications have been published using various techniques of ACL reconstruction, detailed in Table 3. There was no correlation between arterial complications and ACL reconstruction technique, methods of graft fixation or graft type. Eighteen studies reported that the vascular injury was caused by instruments during the ACL reconstruction (shaver, a drill bit for graft fixation, portal incision, previous catheterization and graft harvest). Pseudoaneurysm was the most frequently reported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation. Four studies related their vascular complications to concurrent lateral meniscectomy, PCL reconstruction and preexistent intimal popliteal artery injury due to a previous knee dislocation.

No correlation was found between arterial complications and ACL reconstruction technique, methods of graft fixation or graft type.

(4) What is the time to diagnosis of arterial com-

plications after ACL reconstruction? Six studies reported a time to diagnosis of 0-2 d after ACL reconstruction (Table 3). All other studies showed a certain delay in diagnosis (1-7 wk postsurgery up to 8 years). Contrast-, CT- or MRI- angiographies are the diagnostic tools of choice^[46]. Remarkably, most case reports described palpable dorsalis pedis and posterior tibial arterial pulses at time of clinical presentation with swelling and pain around the popliteal area. These findings have misled surgeons to underestimate vascular complications after ACL reconstruction. Prolonged follow-up and a high level of suspicion, with clinical symptoms of painful pulsating mass and sensory deficits in lower leg and foot, is mandatory in detecting these potentially devastating lesions. An immediate surgical exploration is imperative in limiting neurological damage^[45]. Other than the Gore-Tex rupture ligament case^[31], all patients maintained adequate ACL stability after vascular surgery. The neurological deficits however may be permanent.

The time to diagnosis of arterial complications after ACL reconstruction varies from days to mostly weeks but even years.

Venous complications: (1) What is the incidence of venous thrombo-embolism after ACL reconstruction without thromboprophylaxis? The incidence of VTE after ACL reconstruction without thromboprophylaxis varied from 1.5%-17.9%^[1,58]. The variable incidence of VTE after ACL reconstruction depended on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography) and

Table 5 Incidence venous thromboembolism, risk factors and thromboprophylaxis recommendations

Ref.	Study design	Incidence DVT (symptomatic if specified)	Incidence PE (symptomatic if specified)	Detection method VTE	Risk factors DVT	Thromboprophylaxis recommendations
Marlovits <i>et al</i> ^[20]	RCT	2 = 2.8% with extended prophylaxis; 28 = 41.2% without extended prophylaxis	0%	MRI venography	Comparable between groups	Age > 30, prolonged immobilisation and complex procedures
Mohtadi <i>et al</i> ^[21]	RCT	1 (0.3%) symptomatic	1 (0.3%) symptomatic	Clinical, additional exam in suspected cases	None	-
Adala <i>et al</i> ^[6]	PC	2 = 1.78% (1 pt symptomatic)	0%	Ultrasound preop and day 2-3	None	None if absent high risk factors DVT or age < 45 yr
Cullison <i>et al</i> ^[10]	PC	1 = 1.5%	0%	Ultrasound preop, day 3 and 4 wk	None	None in male patients < 40 yr and absence of risk factors
Hirota <i>et al</i> ^[25]	PC	0%	Peak emboli 50s after tourniquet release	Transoesophageal echocardiography	?	-
Hirota <i>et al</i> ^[22]	PC	0%	0%	Transoesophageal echocardiography	?	-
Lind <i>et al</i> ^[23]	PC	?	?	?	?	-
Maletis <i>et al</i> ^[11]	PC	26 = 0.2% in primary ACLR	15 = < 0.1% in primary ACLR	Various methods	?	?
		2 = 0.2% in revision ACLR	0% in revision ACLR	Idem	?	?
Struijk-Mulder <i>et al</i> ^[5]	PC	9 = 9.0% (symptomatic 4 = 4.0%)	1 = 1%	Bilateral ultrasound	Age, contraceptive use	Further research for DVT prophylaxis, especially when risk factors are present
Williams <i>et al</i> ^[24]	PC	0%	0%	Bilateral ultrasound preop and 7-14 d postop	In 3 patients, non-specified	Future studies needed
Born <i>et al</i> ^[26]	RC	3 = 2.0% symptomatic	?	Clinical, ultrasound in suspected cases	Multiligamentous injury, age, history DVT	In multiligament reconstruction. cf guidelines ACCP "major orthopaedic surgery"
Dong <i>et al</i> ^[8]	RC	17 = 8.5% (44.1% nonsymptomatic of all DVT cases = 12.1% of all patients)	?	Color doppler ultrasound < 24 h after admission and 3 and 7 d postsurgery	Multiligament reconstruction, tourniquet time > 2 h, age	In case of PCL reconstruction and tourniquet time > 2 h
Ettema <i>et al</i> ^[27]	RC	?	?	?	?	None
Gaskill <i>et al</i> ^[2]	RC	55 symptomatic	35	Clinical, additional exam in suspected cases	Age ≥ 35, smoking, cocomitant HTO/ PCL surgery	Further research for VTE prophylaxis
Hetsroni <i>et al</i> ^[30]	RC	?	117 = 0.0003% all symptomatic	Clinical, additional exam in suspected cases	Female gender, age, surgical time, previous cancer	Further research for thromboprophylaxis in high risk patients
Jameson <i>et al</i> ^[28]	RC	42 = 0.3% all symptomatic	25 = 0.8% all symptomatic	Clinical, additional exam in suspected cases	Age > 40	No advise due to lack of evidence
Jaureguito <i>et al</i> ^[7]	RC	Retrospectively clinically 0.24%	0%	Duplex ultrasonography pre-operatively and 5 and 10 d postsurgery	None	-
Sun <i>et al</i> ^[29]	RC	Prospectively 7 (2.9%, 5 asymptomatic = 2.1%) total 36 = 15.6% (4 prox DVT = 2.4%. Distal DVT 32 = 13.9%)	0%	Venography day 3 postsurgery	Age, multiligament surgery	None
Ye <i>et al</i> ^[4]	RC	24 = 14.0% (4 pts prox. DVT)	0%	Chest X-ray and venography day 3 post ACLR	Female gender, age > 35 yr	In female patients and age > 35 yr
Ackerman <i>et al</i> ^[55]	CR	1 = 100%	0%	Clinical, ultrasound, CT and venography	May-Thurner Syndrome	In case of high risk patient
Chien <i>et al</i> ^[50]	CR	?	1 = 100%	Clinical, CT scan	BMI, ACL surgery	Further investigation for thromboprophylaxis after knee arthroscopy needed

Janssen <i>et al</i> ^[47]	CR	1 = 100%	1 = 100%	Clinical, transoesophageal echocardiography	Misdiagnosis DVT, Protein S deficiency? ACL surgery, contraceptive use	Further investigation for thromboprophylaxis after knee arthroscopy needed
Kang <i>et al</i> ^[51]	CR	1 = 100%	0%	Clinical, ultrasound	Primary thrombocytopenia, Factor VIII, Proteine C and S	None
Liu <i>et al</i> ^[52]	CR	1 = 100%	1 = 100%	Clinical, cardiac sonography	BMI	Patients with increased risk and prolonged tourniquet time
Theron <i>et al</i> ^[53]	CR	?	1 = 100%	Clinical, CT	Contraceptive use	None

ACL: ACL reconstruction; BPTB: Bone-patellar tendon-bone; TKA: Total knee arthroplasty; LMWH: Low molecular weight heparin; HTO: High tibial osteotomy; VTE: Venous thromboembolism; PCL: Posterior cruciate ligament; prim: Primary; RCT: Randomized controlled trial; PC: Prospective cohort study; RS: Retrospective study; CR: Case report; CT-scan: Computerized tomography-scan; BMI: Body mass index; DVT: Deep venous thrombosis; ACL: Anterior cruciate ligament; rec.: Reconstruction; pts: Patients; prox.: Proximal.

Table 6 Incidence of venous thromboembolism

Ref.	ACL (n)	Incidence DVT (n)	Incidence sympt DVT (n)	Incidence PE (n)	Thromboprophylaxis	Risk of bias
Adala <i>et al</i> ^[6]	112	2	1	0	No	Low
Cullison <i>et al</i> ^[10]	67	1		0	No	-
Dong <i>et al</i> ^[8]	152	11		NA	No	-
Jameson <i>et al</i> ^[28]	13941	42	42	25	NA	-
Maletis <i>et al</i> ^[11]	15101	26		15	NA	-
Marlovits <i>et al</i> ^[20]	140 (72 vs 68)	2 vs 28		0	Yes	-
Mohtadi <i>et al</i> ^[21]	330	1	1	1	NA	-
Struijk-Mulder <i>et al</i> ^[5]	100	9	4	1	No	Low
Sun <i>et al</i> ^[29]	231	36		0	No	Low
Williams <i>et al</i> ^[24]	23	0	0	0	No	-
Ye <i>et al</i> ^[4]	171	24		0	No	-

Pooled incidence: All DVT: 79/14093 = 9.7%; symptomatic DVT: 5/235 = 2.1%; all DVT of low risk bias studies: 47/443 = 10.6%; PE = 1/704 = 0.1%. ACL: Anterior cruciate ligament reconstruction; DVT: Deep venous thrombosis; sympt: Symptomatic; PE: Pulmonary embolism; NA: Not applicable.

the heterogeneity of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and postoperative mobilisation). Eleven studies reported data of isolated ACL reconstruction without thromboprophylaxis (Table 5). The pooled total incidence of DVT was 9.7%, of which 2.1% was symptomatic. The pooled incidence of DVT in only low-risk bias studies was 10.6%. The pooled incidence of PE was 0.1% (Table 6).

After ACL reconstruction without thromboprophylaxis, the incidence of DVT is 9.7%, of which 2.1% is symptomatic. The incidence of PE is 0.1%.

(2) Is tourniquet time related to VTE after ACL reconstruction? Eight studies that were evaluated by risk of bias analysis documented tourniquet time in ACL reconstruction. This varied from 67.5 min to > 2 h. Deep venous thrombosis was more frequent with tourniquet time > 2 h. Extended tourniquet time was associated with combined ACL reconstruction and concomitant surgery. The incidence of DVT among patients with tourniquet lasting > 2 h increased from 12.1% to 17.4%^[1,58]. In these cases, thromboprophylaxis was recommended with > 2 h tourniquet time.

Tourniquet time > 2 h is related to VTE after ACL reconstruction.

(3) Is thromboprophylaxis indicated after ACL recon-

struction? Eight studies made recommendations for thromboprophylaxis after knee ligament surgery. No thromboprophylaxis was deemed necessary in case of isolated ACL reconstruction in patients without risk factors. Risk factors for VTE were those reported in the ACCP guidelines^[59], female gender, > 30 years of age, complex or concomitant surgical procedures, prolonged immobilization and tourniquet time > 2 h. Further research on thromboprophylaxis is recommended by most authors.

Thromboprophylaxis is indicated in patients considered to be at moderate or high risk of VTE^[20].

DISCUSSION

The most important finding of the present study is that after ACL reconstruction, the incidence of arterial complications, symptomatic DVT and PE was 0.3%, 2.1% and 0.1% respectively. The incidence of 0.3% of arterial complications may be overestimated considering the fact that only case reports have been published in the literature. However, the pooled incidence of DVT after ACL reconstruction without thromboprophylaxis was 9.7%, of which 2.1% of patients was symptomatic.

Pseudaneurysms were the most frequently re-

ported arterial complication after ACL reconstruction, irrespective of graft type or method of graft fixation. Pseudoaneurysms differ from true aneurysms in that they do not contain all the layers of an artery. They resemble organized hematomas that have internal arterial flow^[1]. A direct arterial trauma by a drill bit, shaver, hardware or fixation device for ACL reconstruction may cause a pseudoaneurysm. This condition usually presents with repeated hemarthrosis and a pulsatile mass within days to weeks after ACL reconstruction. Their growth may lead to neuropraxia and DVT due to compression of nerves and nearby veins, respectively^[1]. Patients with poor collateral development may have severe ischemia and poor prognosis, even leading to amputation^[1,35,38].

Krupp *et al.*^[60] analysed the safety of femoral cross-pin in ACL reconstruction. They concluded that insertion angle, not tunnel drilling method, influenced saphenous nerve and femoral artery/vein injury at risk^[60]. Post *et al.*^[61] studied the relative position of the neurovascular structures at risk when drilling bicortical screws for tibial fixation in ACL reconstruction^[45]. Arthroscopic tibial tunnels were made in cadaver human knees using lateral X-rays for accurate positioning. A 4.5 mm bicortical drill hole was placed perpendicular to the tibial surface 1 cm distal to the tibial tunnel. The distances from the posterior tibial drill exit point to the nearby neurovascular structures were measured with a caliper. The closest structure to the exit point was the bifurcation of the popliteal artery/vein (11.4 ± 0.6 mm). The next closest was the anterior tibial vein (11.7 ± 1.6 mm). The closest any individual hole came to a neurovascular structure was 3.5 mm from the anterior tibial vein. They concluded that bicortical screw and spiked washer fixation of soft tissue ACL grafts appears to be relatively safe^[45,61]. Curran *et al.*^[58] performed an *in vitro* study comparing 2 techniques for ACL tibial fixation with a bicortical screw. They concluded that aiming the screw towards the fibula reduced the risk of vascular injury compared to screws drilled perpendicular to the cortex. Other possible recommendations to prevent neurovascular damage are the use of a drill bit stop for bicortical screws or a single cortex fixation on the tibia without compromising stability of fixation^[1]. The incidence of arterial complications in the present review (0.3%)^[45] was updated in a consecutive series of 1961 ACL reconstructions with hamstring autografts and bicortical tibia fixation by the same authors^[1]. The incidence was reduced from 0.3% to 0.15% after the safety measures were applied as suggested by Janssen *et al.*^[1] and Curran *et al.*^[58].

A high level of suspicion, with clinical symptoms of painful pulsating mass and sensory deficits in lower leg and foot, is mandatory in detecting these potentially devastating lesions. The differential diagnosis should include compartment syndrome and DVT^[47]. Doppler examination and intact dorsal pedal and posterior tibial pulses are unreliable in diagnosing arterial lesions after ACL reconstruction^[47]. Contrast-, CT- or MRI-angiographies are the diagnostic tools of choice^[45,46].

Surgical exploration and vascular repair (or ligation/embolization of the feeding vessel) remain standard management^[45,46]. An immediate surgical exploration is imperative in limiting neurological damage^[1,45,46].

A meta-analysis of DVT after knee arthroscopy without thromboprophylaxis found an overall DVT rate of 9.9% (3.1%-17.9%) when routine screening using ultrasound or contrast venography was used^[13]. Proximal DVT rate was 2.1% (0%-4.9%)^[13,62]. Proximal DVT may progress to PE, however the clinical significance of distal DVT remains questionable^[62-64]. Sun *et al.*^[29] found that the total incidence of VTE, diagnosed with venography on the third day after arthroscopic knee surgery, was 14.9%, of which only 3.7% were symptomatic. Delis *et al.*^[14] found 50% of the DVT patients to be completely asymptomatic. They also examined the history of DVT if treated (aspirin in calf DVT, heparin-warfarin in proximal DVT)^[13]. Following early diagnosis, total clot lysis was documented in 50% and partial clot lysis in the remaining 50%, within 118 d median follow-up. Segmental venous reflux developed in at least 75% of the legs sustaining thrombosis. A previous thrombosis or the presence of two or more risk factors for thromboembolism significantly increased the incidence of DVT. No symptoms or signs of PE were documented^[13,14].

The current review showed that after ACL reconstruction without thromboprophylaxis, the incidence of DVT was 9.7%, of which 2.1% was symptomatic. The incidence of PE was 0.1%. These findings are similar to the conclusions by Erickson *et al.*^[3]. They described an 8.4% rate of DVT after ACL reconstructions in patients without postoperative thromboprophylaxis (73% was asymptomatic), while the rate of symptomatic PE was 0.2%^[3]. Maletis *et al.*^[11] described symptomatic DVT in 0.2% of 16192 primary and revision ACL surgeries. However, the authors did not specify the use of thromboprophylaxis^[11]. Cullison *et al.*^[10] and Adala *et al.*^[6] found comparable rates of DVT of 1.5% and 1.8% respectively using prospective pre- and postoperative ultrasonography in patients without VTE risk factors. The authors recommended that thromboprophylaxis is not necessary in the absence of risk factors in patients younger than 45 years of age with early postoperative mobilization^[6]. In a study of 282 Chinese patients, the incidence of DVT was 12.1% after ACL reconstruction. Tourniquet time > 2 h and concomitant PCL reconstructions were risk factors for DVT^[8]. Ye *et al.*^[4] found that the incidence of DVT was 14%, diagnosed by unilateral venography on the third day after ACL reconstruction. Proximal DVT occurred in 16.7% of DVT patients. None of the DVT patients developed PE. The authors recommended thromboprophylaxis in female patients and patients older than 35 years^[4]. The described variable incidence of VTE after ACL reconstruction depends on the diagnostic methods of DVT (clinical parameters, venography, ultrasound or magnetic resonance venography) and the heterogeneity

of patient demographics (age, risk factors, surgical time, concomitant surgery, tourniquet time and postoperative immobilization).

The use of a tourniquet improves operative visualization during arthroscopic ACL reconstruction^[65,66]. Various authors reported that tourniquet time in excess of 90 min increased the rates of VTE^[8,17,30,67]. Smith *et al.*^[65] published a meta-analysis of tourniquet assisted arthroscopic knee surgery. There was no difference in complication rate if tourniquet time exceeded 60 min. Hirota *et al.*^[22,25] quantified pulmonary emboli after tourniquet release in patients during ACL reconstruction (extramedullary) vs total knee arthroplasty (intramedullary procedure)^[13]. They chose these two groups for having more than 60 min tourniquet time and detected pulmonary emboli in all patients after release of the tourniquet using transesophageal echocardiography with a peak at 30-40 s postrelease^[13]. The amount of emboli was defined as percentage of total emboli formed in relation to the right atrial area. This percentage returned to baseline levels 2 min after tourniquet release in the ACL group. They found a significant linear correlation between the amount of emboli and duration of tourniquet inflation in the ACL group. In comparison, the total knee arthroplasty group had a significant larger amount of emboli (4-5 fold) with no return to baseline levels during the assessment period. No patient in either group showed signs of PE^[13,22,25]. In a recent systematic review, Papalia *et al.*^[66] concluded that a tourniquet can be used safely, provided that the inflation pressure is not excessive and tourniquet time is less than 2 h.

Asymptomatic pulmonary emboli occur in all patients with ACL reconstructions after tourniquet release^[1,13]. Furthermore, PE may occur as a result of proximal DVT^[13,24,50,52]. Hetsroni *et al.*^[30] analysed 418323 arthroscopic knee procedures and found an incidence of 0.03% for symptomatic PE. Risk factors were female sex, age, history of cancer and prolonged operating time (> 90 min). In spite of improved prevention and treatment of PE, the mortality is still estimated to be 20%-30%^[68]. It is the third most common cardiovascular cause of death, with 2/3 of the death occurring within the first few hours as a result of severe hemodynamic and respiratory disturbances^[53,68,69]. Janssen *et al.*^[1,13] found an incidence of fatal PE of 0.05% in a consecutive series of 1961 arthroscopic ACL reconstructions^[1]. Risk factors were preexistent coagulopathy, oral contraceptive medication and delay in DVT diagnosis.

Thromboprophylaxis after ACL reconstruction remains controversial^[1,9,16,27,50,52,59,70,71]. Geerts *et al.*^[59] reviewed the evidence-based literature for thromboprophylaxis in knee arthroscopy and only recommend prophylaxis with Low Molecular Weight Heparin in patients with risk factors for VTE (Grade 2B level of evidence). Risk factors in their study were history of DVT, age \geq 40 years, surgical time > 60 min. and a complicated/prolonged procedure^[59]. Additional risk factors for VTE after ACL reconstruction in other studies on VTE were smoking, oral contraceptive use

or hormone replacement, BMI > 30 kg/m², chronic venous insufficiency, cancer and thrombophilic conditions^[1,12,14,30,52,59,64,72]. In a randomized controlled trial, Marlovits *et al.*^[20] concluded that extended duration of thromboprophylaxis with enoxaparin by an additional 20 d significantly reduced venographically detected DVT after ACL reconstruction without an increase in major bleeding compared to enoxaparin limited to in-hospital thromboprophylaxis for 3-8 d. The authors found a 41.2% incidence of DVT for discharged patients who had a placebo as postdischarge thromboprophylaxis in contrast to 2.8% in the thromboprophylaxis group. Risk factors for DVT were age over 30 years, prolonged immobilization and surgical time^[20]. It should be noted that their mean surgical time as a teaching hospital (> 2 h) as well as their hospital stay of 3-8 d do not reflect most current ACL surgery practices with early discharge and mobilization. A Cochrane systematic review on interventions for preventing VTE in adults undergoing knee arthroscopy reported that no strong evidence was found to conclude that thromboprophylaxis is effective to prevent VTE in people with unknown risk factors for thrombosis^[20,68,70]. This is confirmed by other recent studies on DVT prophylaxis after ACL reconstruction and knee arthroscopic procedures^[2,17,64]. It is now common practice in a surgical setting to use a risk-assessment model, such as the one developed by Capriani *et al.*^[20]. Patients considered to be at moderate or high risk of VTE should routinely receive thromboprophylaxis^[1]. However, recommendations for the best type and duration of prophylaxis after ACL reconstruction still need to be defined^[5]. In spite of the scientific effort to date, no recommendations for routine thromboprophylaxis in ACL reconstruction can be provided in the absence of risk factors for VTE^[1,13]. Further investigation is required to analyse actual incidence and severity of venous thromboembolism as well as the efficacy-to-bleeding tradeoff for routine thromboprophylaxis after ACL reconstruction in patients without risk factors for VTE^[1,13].

This systematic review has several limitations. In the search for the available knowledge on vascular complications, studies of various level of evidence were included. Another weakness of this review is the inclusion of studies with small population size. Both the quality and limited amount of studies for specific research questions may limit the level of evidence for this review. Although strict and adapted for various study types, the risk of bias assessment of the Cochrane Library and the classifications of "low", "questionable" and "high" risk of bias for the studies may limit the strength of evidence. One might argue that a "low" risk of bias RCT study is of higher level of evidence than a "low" risk of bias prospective cohort study. Another weakness of this study is that only articles in English were included. Additional relevant articles published in languages other than English could contribute to the level of evidence presented in this review.

The clinical relevance of this review is that patients

undergoing ACL reconstruction may be informed that vascular complications can occur with any type of reconstruction and that thromboprophylaxis should be prescribed in patients with risk factors for VTE.

After ACL reconstruction, the incidence of arterial complications, symptomatic DVT and PE was 0.3%, 2.1% and 0.1% respectively. Arterial complications may occur with all types of arthroscopic ACL reconstruction, methods of graft fixation as well as any type of graft. Patients considered to be at moderate or high risk of VTE should routinely receive thromboprophylaxis after ACL reconstruction.

COMMENTS

Background

A thorough understanding of the incidence, risk factors and potential methods for prevention of vascular complications after anterior cruciate ligament (ACL) reconstruction is critical to optimize patient safety. This systematic review presents the current knowledge of arterial complications, venous thromboembolism (VTE) and thromboprophylaxis after arthroscopic ACL reconstruction. The review highlights the incidence, types and risk factors of arterial complications and VTE after ACL reconstruction as well as the current recommendations for deep venous thrombosis prophylaxis.

Research frontiers

This systematic review is related to research on thromboprophylaxis after ACL reconstruction.

Innovations and breakthroughs

This review presents a systematic overview of the incidence and type of arterial complications after ACL reconstruction. Such an overview has not been presented previously. Furthermore, an overview of the incidence, risk factors and indications for thromboprophylaxis after ACL reconstruction are presented. There is a need for this current knowledge due to the controversy in this field of research. Suggestions for further research are presented in the study.

Applications

Clinical implications are presented for adequate diagnosis and treatment of vascular complications after ACL reconstruction. Risk factors and indications for thromboprophylaxis are discussed.

Terminology

All terminology is explained in the manuscript.

Peer-review

This is an interesting systematic review that aims to evaluate the arterial and venous complications, by analyzing the relevant studies.

REFERENCES

- 1 **Janssen RP**, Reijman M, Janssen DM, Mourik van JBA. Vascular complications after ACL reconstruction and DVT prophylaxis. In: Prodromos CC editor. *The anterior cruciate ligament. Reconstruction and basic science*, Philadelphia, USA: Saunders, an imprint of Elsevier, 2015
- 2 **Gaskill T**, Pullen M, Bryant B, Sicignano N, Evans AM, DeMaio M. The Prevalence of symptomatic deep venous thrombosis and pulmonary embolism after anterior cruciate ligament reconstruction. *Am J Sports Med* 2015; **43**: 2714-2719 [PMID: 26391861 DOI: 10.1177/0363546515601970]
- 3 **Erickson BJ**, Saltzman BM, Campbell KA, Fillingham YA, Harris JD, Gupta AK, Bach BR. Rates of deep venous thrombosis and pulmonary embolus after anterior cruciate ligament reconstruction: a systematic review. *Sports Health* 2015; **7**: 261-266 [PMID: 26131305 DOI: 10.1177/1941738115576927]
- 4 **Ye S**, Dongyang C, Zhihong X, Dongquan S, Jin D, Jianghui Q, Jizhen Q, Pu Y, Huacheng H, Wei S, Qing J. The incidence of deep venous thrombosis after arthroscopically assisted anterior cruciate ligament reconstruction. *Arthroscopy* 2013; **29**: 742-747 [PMID: 23527593 DOI: 10.1016/j.arthro.2013.01.017]
- 5 **Struijk-Mulder MC**, Ettema HB, Verheyen CC, Büller HR. Deep vein thrombosis after arthroscopic anterior cruciate ligament reconstruction: a prospective cohort study of 100 patients. *Arthroscopy* 2013; **29**: 1211-1216 [PMID: 23809456 DOI: 10.1016/j.arthro.2013.04.015]
- 6 **Adala R**, Anand A, Kodikal G. Deep vein thrombosis and thromboprophylaxis in arthroscopic anterior cruciate ligament reconstruction. *Indian J Orthop* 2011; **45**: 450-453 [PMID: 21886928 DOI: 10.4103/0019-5413.83952]
- 7 **Jaureguito JW**, Greenwald AE, Wilcox JF, Paulos LE, Rosenberg TD. The incidence of deep venous thrombosis after arthroscopic knee surgery. *Am J Sports Med* 1999; **27**: 707-710 [PMID: 10569354]
- 8 **Dong JT**, Wang X, Men XQ, Wang XF, Zheng XZ, Gao SJ. Incidence of deep venous thrombosis in Chinese patients undergoing arthroscopic knee surgery for cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3540-3544 [PMID: 25362246 DOI: 10.1007/s00167-014-3216-x]
- 9 **Schippinger G**, Wirnsberger GH, Obernosterer A, Babinski K. Thromboembolic complications after arthroscopic knee surgery. Incidence and risk factors in 101 patients. *Acta Orthop Scand* 1998; **69**: 144-146 [PMID: 9602771]
- 10 **Cullison TR**, Muldoon MP, Gorman JD, Goff WB. The incidence of deep venous thrombosis in anterior cruciate ligament reconstruction. *Arthroscopy* 1996; **12**: 657-659 [PMID: 9115551 DOI: 10.1016/s0749-8063(96)90166-8]
- 11 **Maletis GB**, Inacio MC, Funahashi TT. Analysis of 16,192 anterior cruciate ligament reconstructions from a community-based registry. *Am J Sports Med* 2013; **41**: 2090-2098 [PMID: 23813802 DOI: 10.1177/0363546513493589]
- 12 **Montesinos-Berry E**, Sanchis-Alfonso V. Deep venous thrombosis and pulmonary embolism after acl reconstruction: What can we do to prevent it? In: Sanchis Alfonso V, Monllau JC, editors. *The acl-deficient knee*, London, Springer-Verlag, 2013: 391-399
- 13 **Janssen RP**, Sala HA. Fatal pulmonary embolism after anterior cruciate ligament reconstruction. *Am J Sports Med* 2007; **35**: 1000-1002 [PMID: 17307895 DOI: 10.1177/0363546506298581]
- 14 **Delis KT**, Hunt N, Strachan RK, Nicolaides AN. Incidence, natural history and risk factors of deep vein thrombosis in elective knee arthroscopy. *Thromb Haemost* 2001; **86**: 817-821 [PMID: 11583313]
- 15 **Nordenvall R**, Bahmanyar S, Adami J, Stenros C, Wredmark T, Felländer-Tsai L. A population-based nationwide study of cruciate ligament injury in Sweden, 2001-2009: incidence, treatment, and sex differences. *Am J Sports Med* 2012; **40**: 1808-1813 [PMID: 22684536 DOI: 10.1177/0363546512449306]
- 16 **Struijk-Mulder MC**, Ettema HB, Verheyen CC, Büller HR. Comparing consensus guidelines on thromboprophylaxis in orthopedic surgery. *J Thromb Haemost* 2010; **8**: 678-683 [PMID: 20040041 DOI: 10.1111/j.1538-7836.2009.03728.x]
- 17 **Bogunovic L**, Jain A, Campbell KA, Wright RW. The role of DVT prophylaxis after ACL reconstruction. *Oper Tech Sports Med* 2015; Epub ahead of print [DOI: 10.1053/j.otsm.2015.09.003]
- 18 **Liberati A**, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009; **62**: e1-34 [PMID: 19631507 DOI: 10.1016/j.jclinepi.2009.06.006]
- 19 **Checklist of the Dutch Cochrane centre**. Checklist of etiology and harm. In: Offringa M, Assendel WJJ, Scholten RJPM, editors. *Inleiding in evidence-based medicine*, Bohn Stafleu van Loghum, Springer media: 2014
- 20 **Marlovits S**, Striessnig G, Schuster R, Stocker R, Luxl M, Trattinig S, Vécsei V. Extended-duration thromboprophylaxis with enoxaparin

- after arthroscopic surgery of the anterior cruciate ligament: a prospective, randomized, placebo-controlled study. *Arthroscopy* 2007; **23**: 696-702 [PMID: 17637403 DOI: 10.1016/j.arthro.2007.02.001]
- 21 **Mohtadi N**, Barber R, Chan D, Paolucci EO. Complications and adverse events of a randomized clinical trial comparing 3 graft types for ACL reconstruction. *Clin J Sport Med* 2016; **26**: 182-189 [PMID: 25881568]
 - 22 **Hirota K**, Hashimoto H, Tsubo T, Ishihara H, Matsuki A. Quantification and comparison of pulmonary emboli formation after pneumatic tourniquet release in patients undergoing reconstruction of anterior cruciate ligament and total knee arthroplasty. *Anesth Analg* 2002; **94**: 1633-1638, table of contents [PMID: 12032043]
 - 23 **Lind M**, Menhert F, Pedersen AB. The first results from the Danish ACL reconstruction registry: epidemiologic and 2 year follow-up results from 5,818 knee ligament reconstructions. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 117-124 [PMID: 18974970 DOI: 10.1007/s00167-008-0654-3]
 - 24 **Williams JS**, Hulstyn MJ, Fadale PD, Lindy PB, Ehrlich MG, Cronan J, Dorfman G. Incidence of deep vein thrombosis after arthroscopic knee surgery: a prospective study. *Arthroscopy* 1995; **11**: 701-705 [PMID: 8679032]
 - 25 **Hirota K**, Hashimoto H, Kabara S, Tsubo T, Sato Y, Ishihara H, Matsuki A. The relationship between pneumatic tourniquet time and the amount of pulmonary emboli in patients undergoing knee arthroscopic surgeries. *Anesth Analg* 2001; **93**: 776-780 [PMID: 11524355]
 - 26 **Born TR**, Engasser WM, King AH, Krych AJ, Dahm DL, Levy BA, Stuart MJ. Low frequency of symptomatic venous thromboembolism after multiligamentous knee reconstruction with thromboprophylaxis. *Clin Orthop Relat Res* 2014; **472**: 2705-2711 [PMID: 24696048 DOI: 10.1007/s11999-014-3576-z]
 - 27 **Ettema HB**, Mulder MC, Nurmohamed MT, Büller HR, Verheyen CC. Dutch orthopedic thromboprophylaxis: a 5-year follow-up survey. *Acta Orthop* 2009; **80**: 109-112 [PMID: 19234891 DOI: 10.1080/17453670902807441]
 - 28 **Jameson SS**, Dowen D, James P, Serrano-Pedraza I, Reed MR, Deehan D. Complications following anterior cruciate ligament reconstruction in the English NHS. *Knee* 2012; **19**: 14-19 [PMID: 21216599 DOI: 10.1016/j.knee.2010.11.011]
 - 29 **Sun Y**, Chen D, Xu Z, Shi D, Dai J, Qin J, Jiang Q. Incidence of symptomatic and asymptomatic venous thromboembolism after elective knee arthroscopic surgery: a retrospective study with routinely applied venography. *Arthroscopy* 2014; **30**: 818-822 [PMID: 24768465 DOI: 10.1016/j.arthro.2014.02.043]
 - 30 **Hetsroni I**, Lyman S, Do H, Mann G, Marx RG. Symptomatic pulmonary embolism after outpatient arthroscopic procedures of the knee: the incidence and risk factors in 418,323 arthroscopies. *J Bone Joint Surg Br* 2011; **93**: 47-51 [PMID: 21196542 DOI: 10.1302/0301-620X.93B1.25498]
 - 31 **Spalding TJ**, Botsford DJ, Ford M, Marks PH. Popliteal artery compression: a complication of Gore-Tex anterior cruciate ligament reconstruction. *J Bone Joint Surg Br* 1996; **78**: 151-152 [PMID: 8898150]
 - 32 **Aldridge JM**, Weaver JP, Mallon WJ. Avulsion of the middle genicular artery: a previously unreported complication of anterior cruciate ligament repair. A case report. *Am J Sports Med* 2000; **30**: 748-750 [PMID: 12239013]
 - 33 **Evans JD**, de Boer MT, Mayor P, Rees D, Guy AJ. Pseudoaneurysm of the medial inferior genicular artery following anterior cruciate ligament reconstruction. *Ann R Coll Surg Engl* 2000; **82**: 182-184 [PMID: 10858680]
 - 34 **Friederich NF**, Czaja S. Recurrent acute hemarthrosis after anterior cruciate ligament reconstruction. Report of an unusual complication and a review of the literature. *Knee Surg Sports Traumatol Arthrosc* 1996; **3**: 215-218 [PMID: 8739716 DOI: 10.1007/BF01466620]
 - 35 **Kanko M**, Buluc L, Yavuz S, Muezzinoglu S, Berki T. Very rare aetiology of giant popliteal pseudoaneurysm: anterior cruciate ligament surgery. *Postgrad Med J* 2008; **84**: 158-159 [PMID: 18372488 DOI: 10.1136/pgmj.2007.062646]
 - 36 **Keçeci B**, Küçük L, Biçer EK, Posacioğlu H. Traumatic arteriovenous fistula formation after misplaced femoral tunnel in arthroscopic anterior cruciate ligament reconstruction. *Eklemler Hastalik Cerrahisi* 2012; **23**: 117-120 [PMID: 22765493]
 - 37 **Lamo-Espinosa JM**, Llombart Blanco R, Valentí JR. Inferior lateral genicular artery injury during anterior cruciate ligament reconstruction surgery. *Case Rep Surg* 2012; **2012**: 457198 [PMID: 22957293 DOI: 10.1155/2012/457198]
 - 38 **Mello W**, de Brito WE, Migon EZ, Borges A. Pseudoaneurysm of the medial inferior genicular artery after anterior cruciate ligament reconstruction. *Arthroscopy* 2011; **27**: 442-445 [PMID: 21353173 DOI: 10.1016/j.arthro.2010.10.015]
 - 39 **Pereira ED**, Mestriner LA, Pereira ED, Domingues RP, Cardoso MPA. Geniculate artery pseudoaneurysm after arthroscopic knee surgery: Two case reports. *Acta Ortopedica Brasileira* 2010; **18**: 104-106
 - 40 **Roth JH**, Bray RC. Popliteal artery injury during anterior cruciate ligament reconstruction: brief report. *J Bone Joint Surg Br* 1988; **70**: 840 [PMID: 3192593]
 - 41 **Tam Kelvin KW**, Wun YC, Lau CY, Chow YY. Pseudoaneurysm of the popliteal artery after anterior cruciate ligament reconstruction surgery: A case report and literature review. *J Orthop Traum Rehabil* 2014; **18**: 44-46 [DOI: 10.1016/j.jotr.2013.12.001]
 - 42 **Lee GC**, Kim DH, Park SH. Popliteal artery pseudoaneurysm after anterior cruciate ligament re-revision using a rigidfix cross pin. *Knee Surg Relat Res* 2014; **26**: 121-124 [PMID: 24944979 DOI: 10.5792/ksrr.2014.26.2.121]
 - 43 **Buda R**, Mosca M, Di Caprio F, Ruffilli A, Rossi G, Giannini S. Pseudoaneurysm in a segmental branch of the posterior tibial artery following knee ligament reconstruction in a patient with favism. *Medicina Dello Sport* 2008; **61**: 65-70
 - 44 **Galanakis I**, Aligizakis A, Giannoukas A, Katsamouris A, Katonis P, Hadjipavlou A. Popliteal artery injury, peroneal nerve neuropathy and tibial nerve transection of the right knee, after an arthroscopic assisted anterior cruciate ligament reconstruction. *Minerva Ortop Traumatol* 2003; **54**: 39-43
 - 45 **Janssen RP**, Scheltinga MR, Sala HA. Pseudoaneurysm of the popliteal artery after anterior cruciate ligament reconstruction with bicortical tibial screw fixation. *Arthroscopy* 2004; **20**: E4-E6 [PMID: 14716289]
 - 46 **Janssen RP**, Sala H, Prakken WJ. Simultaneous traumatic pseudoaneurysm and thrombosis of the popliteal artery after anterior cruciate ligament reconstruction. *Injury Extra* 2007; **38**: 397-399
 - 47 **Janssen RP**, Sala HA. Embolism of the popliteal artery after anterior cruciate ligament reconstruction: a case report and literature review. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 1449-1451 [PMID: 17579836 DOI: 10.1007/s00167-007-0363-3]
 - 48 **Milankov M**, Miljkovic N, Stankovic M. Pseudoaneurysm of the medial inferior genicular artery following anterior cruciate ligament reconstruction with hamstring tendon autograft. *Knee* 2006; **13**: 170-171 [PMID: 16458515 DOI: 10.1016/j.knee.2005.12.002]
 - 49 **Carr JB**, Jansson KA. An unusual case of vascular dysplasia related to knee arthroscopy. *Arthroscopy* 2001; **17**: 196-199 [PMID: 11172250 DOI: 10.1053/jars.2001.8021]
 - 50 **Chien SC**, Tsai JP, Yen CH, Kuo JY, Hung CL. Severe pulmonary embolism in a young man post knee arthroscopic anterior cruciate ligament repair: A case report and literature review. *J Intern Med Taiwan* 2012; **23**: 106-113
 - 51 **Kang H**, Cao J, Yu D. Deep vein thrombosis after arthroscopic anterior cruciate ligament reconstruction in a patient with primary thrombocytopenia. *Acta Orthop Traumatol Turc* 2014; **48**: 455-458 [PMID: 25230271 DOI: 10.3944/AOTT.2014.3024]
 - 52 **Liu YC**, Chang TK, Liu SC, Lu YC. Pulmonary embolism manifested as acute coronary syndrome after arthroscopic anterior cruciate ligament reconstruction. *Formos J Musculoskelet Disord* 2013; **4**: 72-75 [DOI: 10.1016/j.fjmd.2013.03.002]
 - 53 **Theron C**, Laidlow DC. Life threatening massive pulmonary embolism treated with reteplase: a case report. *Crit Care Resusc* 2000; **2**: 278-281 [PMID: 16597314]
 - 54 **Tsubosaka M**, Matsushita T, Kuroda R, Matsumoto T, Kurosawa M. Pseudoaneurysm of the articular branch of the descending

- genicular artery following double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015; Epub ahead of print [PMID: 25986096]
- 55 **Ackerman J**, Kurdziel MD. Extensive lower-extremity deep venous thrombosis following arthroscopic anterior cruciate ligament reconstruction related to may-thumer syndrome. *JBJS Case Connect* 2015; **5**: e49
- 56 **Panigrahi R**, Mahapatra AK, Palo N, Priyadarshi A. Thrombotic popliteal block following simultaneous bi-cruciate single-stage arthroscopic reconstruction in a neglected multiligamentous knee injury in a smoker. *BMJ Case Rep* 2015; **2015**: [PMID: 26150635 DOI: 10.1136/bcr-2015-209933]
- 57 **Ambrosia J**, Qazi Z, Shuler FD, Giangarra C. Delayed pseudoaneurysm of the popliteal artery following ACL reconstruction. *Orthopedics* 2015; **38**: e543-e546 [PMID: 26091231 DOI: 10.3928/01477447-20150603-93]
- 58 **Curran TA**, Sekiya JK, Gibbs AE, Bonner KF. Two techniques for anterior cruciate ligament tibial fixation with a bicortical screw: an in vitro study of neurovascular risk. *Am J Orthop (Belle Mead NJ)* 2006; **35**: 261-264 [PMID: 16841787]
- 59 **Geerts WH**, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; **133**: 381S-453S [PMID: 18574271 DOI: 10.1378/chest.08-0656]
- 60 **Krupp R**, Scovell F, Cook C, Nyland J, Wyland D. Femoral cross-pin safety in anterior cruciate ligament reconstruction as a function of femoral tunnel position and insertion angle. *Arthroscopy* 2011; **27**: 83-88 [PMID: 20952148 DOI: 10.1016/j.arthro.2010.06.030]
- 61 **Post WR**, King SS. Neurovascular risk of bicortical tibial drilling for screw and spiked washer fixation of soft-tissue anterior cruciate ligament graft. *Arthroscopy* 2001; **17**: 244-247 [PMID: 11239343 DOI: 10.1053/jars.2001.21539]
- 62 **Ilahi OA**, Reddy J, Ahmad I. Deep venous thrombosis after knee arthroscopy: a meta-analysis. *Arthroscopy* 2005; **21**: 727-730 [PMID: 15944631 DOI: 10.1016/j.arthro.2005.03.007]
- 63 **Hoppener MR**, Ettema HB, Henny CP, Verheyen CC, Büller HR. Low incidence of deep vein thrombosis after knee arthroscopy without thromboprophylaxis: a prospective cohort study of 335 patients. *Acta Orthop* 2006; **77**: 767-771 [PMID: 17068708 DOI: 10.1080/17453670610012962]
- 64 **Krych AJ**, Sousa PL, Morgan JA, Levy BA, Stuart MJ, Dahm DL. Incidence and risk factor analysis of symptomatic venous thromboembolism after knee arthroscopy. *Arthroscopy* 2015; **31**: 2112-2118 [PMID: 26105091 DOI: 10.1016/j.arthro.2015.04.091]
- 65 **Smith TO**, Hing CB. A meta-analysis of tourniquet assisted arthroscopic knee surgery. *Knee* 2009; **16**: 317-321 [PMID: 19239987 DOI: 10.1016/j.knee.2009.01.004]
- 66 **Papalia R**, Zampogna B, Franceschi F, Torre G, Maffulli N, Denaro V. Tourniquet in knee surgery. *Br Med Bull* 2014 May 17; Epub ahead of print [PMID: 24837461 DOI: 10.1093/bmb/ldu012]
- 67 **Demers C**, Marcoux S, Ginsberg JS, Laroche F, Cloutier R, Poulin J. Incidence of venographically proved deep vein thrombosis after knee arthroscopy. *Arch Intern Med* 1998; **158**: 47-50 [PMID: 9437378]
- 68 **College of Intensive Care Medicine**. Available from: URL: <http://www.cicm.org.au>
- 69 **Tebbe U**, Graf A, Kamke W, Zahn R, Forycki F, Kratzsch G, Berg G. Hemodynamic effects of double bolus reteplase versus alteplase infusion in massive pulmonary embolism. *Am Heart J* 1999; **138**: 39-44 [PMID: 10385761]
- 70 **Ramos J**, Perrotta C, Badariotti G, Berenstein G. Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy. *Cochrane Database Syst Rev* 2008; **(4)**: CD005259 [PMID: 18843687 DOI: 10.1002/14651858.CD005259.pub3]
- 71 **Squizzato A**, Ageno W. The 8(th) American College of Chest Physicians Guidelines - a perspective on venous thromboembolism guidelines. *Thromb Haemost* 2009; **101**: 31-35 [PMID: 19132186]
- 72 **Cancienne JM**, Gwathmey FW, Miller MD, Werner BC. Tobacco use is associated with increased complications after anterior cruciate ligament reconstruction. *Am J Sports Med* 2016; **44**: 99-104 [PMID: 26526974 DOI: 10.1177/0363546515610505]

P- Reviewer: de Campos GC, Paschos NK, Seijas R **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Wu HL



Compartment syndrome following total knee replacement: A case report and literature review

Mohammed Shaath, Mohamed Sukeik, Saadallah Mortada, Sean Masterson

Mohammed Shaath, Department of Trauma and Orthopaedics, North Manchester General Hospital, Crumpsall M8 5RB, United Kingdom

Mohamed Sukeik, Saadallah Mortada, Sean Masterson, Department of Trauma and Orthopaedics, Queens Hospital, Romford RM7 0AG, United Kingdom

Author contributions: Shaath M and Sukeik M designed the report; Sukeik M, Mortada S and Masterson S collected the patient's clinical data; Shaath M, Sukeik M, Mortada S and Masterson S analyzed the data; Shaath M and Sukeik M wrote the paper.

Institutional review board statement: This case report was exempt from the Institutional Review Board standards at Queens Hospital.

Informed consent statement: Unfortunately in December 2014, the patient died from causes unrelated to the contents of this case report. Written consent was therefore not obtained despite the patient verbally agreeing to publish it in the immediate postoperative phase. However, in light of the importance of the article message, we have included no identifiable patient information and feel this report should still be published.

Conflict-of-interest statement: There is no conflict of interest for any of the authors

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Mohamed Sukeik, MD, MRCSEd, PGA, Specialist Registrar in Trauma and Orthopaedics, Department of Trauma and Orthopaedics, Queens Hospital, Rom Valley Way, Romford RM7 0AG, United Kingdom. msukeik@hotmail.com

Telephone: +44-208-9542300
Fax: +44-127-9827672

Received: March 29, 2016
Peer-review started: March 29, 2016
First decision: May 17, 2016
Revised: May 29, 2016
Accepted: July 11, 2016
Article in press: July 13, 2016
Published online: September 18, 2016

Abstract

Compartment syndrome is a rare complication of total knee replacement (TKR) surgery that needs prompt diagnosis and treatment as it may be associated with high morbidity and mortality. We have found very few reports in the literature describing compartment syndrome after TKRs and therefore, present a relevant case which occurred in the immediate postoperative phase and was treated with fasciotomy and subsequent operations to close the soft tissue defects.

Key words: Compartment syndrome; Complications; Knee replacement; Treatment

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A case report and literature review of compartment syndrome following total knee replacement surgery is presented. Predisposing factors supported by literature are detailed and compared to findings from this case report emphasizing on early intervention to prevent subsequent complications.

Shaath M, Sukeik M, Mortada S, Masterson S. Compartment syndrome following total knee replacement: A case report and literature review. *World J Orthop* 2016; 7(9): 618-622 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/618>.

INTRODUCTION

Compartment syndrome is a serious condition that occurs due to elevation of interstitial pressure in closed fascial compartments resulting in microvascular compromise, myoneuronal function impairment and soft tissue necrosis. Fractures, crush injuries, vascular injuries, prolonged tourniquet application, anticoagulation and deep-vein thrombosis have all been associated with compartment syndrome^[1], with fractures and soft tissue injuries accounting for approximately 80% of all cases. Pain out of proportion and pain on passive stretching of the affected compartment have been described as the most reliable clinical indicators of compartment syndrome. These symptoms alongside palor, pulselessness, paraesthesia and paralysis are characteristic for compartment syndrome. Paraesthesia and paralysis arise as a result of significant compartmental ischaemia, after which a full recovery becomes unlikely^[1].

The increase in intracompartmental pressures can be measured using the Wick catheter technique^[2] or a handheld manometer. A manometer device attached to a needle is inserted into each compartment to provide a pressure reading. A normal compartmental pressure reflects the capillary pressure of 0 to 8 mmHg. When measured, an intracompartmental pressure of 30 mmHg and delta (differential) pressure of 30 mmHg or less are used as an indication for fasciotomy^[3].

Despite the relative scarcity in the incidence of compartment syndrome following total knee replacement (TKR), it remains an important complication which may potentially be limb as well as life threatening.

We hereby, present a case of a compartment syndrome which occurred following TKR surgery and discuss the potential factors which may have contributed to its development.

CASE REPORT

In May 2013, a 72-year-old white British lady with background of chronic obstructive pulmonary disease (COPD), hypertension, prior pulmonary embolism, oesophagitis and cataracts was admitted with a diagnosis of primary osteoarthritis for an elective right TKR. Her medications included spiriva 18 mcg, uniphyllin 200 mg, ramipril 1.25 mg, folic acid 5 mg, amlodipine 10 mg, ipratropium 500 mcg, omeprazole 20 mg and salbutamol inhaler and she had no medication allergy. The patient occasionally also used home oxygen therapy for COPD exacerbations. Past surgical history included epistaxis needing cautery, duodenal ulcer surgery and gastroscopy. Family history was insignificant. She was a housewife and lived alone, a previously heavy smoker but stopped one year prior to her presentation and drank alcohol occasionally. Her clinical examination confirmed tenderness over the medial and lateral knee

compartments as well as the retropatellar region with a range of movement from 0-120 degrees of flexion. There were no signs of neurological deficit or vascular compromise in the lower limbs. Radiographs taken pre-operatively showed tricompartmental osteoarthritis. Her ASA grading was 3^[4]. The surgical procedure was performed as per the surgeon's routine practice under a spinal/epidural anaesthetic. Patient had three doses of perioperative cefuroxime as per hospital antibiotic prophylaxis guidelines. After elevation of the limb, a pneumatic tourniquet around the upper part of the thigh was inflated to a pressure of 300 mmHg. A midline skin incision and medial parapatellar approach were utilised to expose the knee joint. Standard surgical techniques for intraoperative haemostasis were used. A cemented Columbus[®] TKR was implanted. After all components were cemented into place, a thorough washout with normal saline was performed and the wound was closed in layers. No surgical drain was used. The tourniquet was released after the application of dressings. Tourniquet time was 90 min. Forty mgs of dexane (enoxaparin) was given on the day of surgery with the plan to continue for 4 wk. The patient returned to the recovery unit where an anteroposterior and lateral X-rays of her right knee were performed as per departmental protocol (Figure 1). After an uneventful recovery, she was transferred to the ward to undergo rehabilitation. The following day she started complaining of pain in the right lower leg which by midday became excruciating and was exacerbated by any passive movement of the toes. The patient experienced tension across the entirety of the calf as well as paraesthesia. The distal pulses in the leg were palpable but weak. A clinical diagnosis of compartment syndrome of the leg was made based on these clinical findings and a Stryker Intra-Compartmental Pressure Monitor measured pressures of 26, 32 and 42 mmHg in the anterior, lateral and posterior compartments respectively (Figure 2).

Therefore she was taken immediately to the operating theatre and a decompression of all 4 compartments was performed using lateral and medial longitudinal incisions. Post fasciotomies the blood supply to the muscles which were deemed viable at the time of surgery was restored and pain was markedly relieved. The patient had to go back to theatre three times subsequently in order to completely close the wounds. The lateral incision was closed 3 d postoperatively while the medial incision was closed 3 wk later after a period of vacuum pump application.

The patient was followed up as an inpatient until complete closure of all wounds. On further examination, she was mobilizing fully weightbearing with no restrictions and achieved a range of movement from 0-95 degrees of flexion. At 12 mo follow-up appointment, the patient maintained her good functional outcome with no neurovascular deficit in the right lower limb and hence got discharged. However, in December 2014, she died from respiratory failure secondary to lung cancer. Reviewing her case notes did not show any deterioration

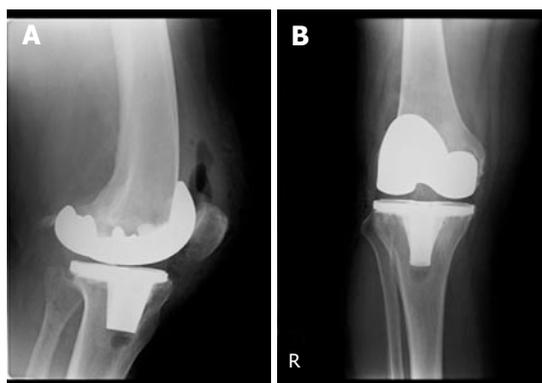


Figure 1 Immediate postoperative X-rays of the total knee replacement in recovery (A and B).



Figure 2 The Stryker Intra-Compartmental Pressure Monitor is a hand held monitor for measurement of compartmental pressure.

of her knee prior to her death.

Literature review

Owing to the rarity of this complication, a comprehensive literature review aiming to identify contributing factors was conducted. The exploded MeSH terms “total knee replacement” and “Compartment syndrome” were used to search MEDLINE and EMBASE databases for relevant articles in English. Two authors independently reviewed the titles and abstracts and when in doubt the full articles were retrieved and reviewed to reach consensus. Following this irrelevant studies were excluded. We included only cases where a unilateral primary TKR was performed to provide direct comparisons with the current case report. This yielded 12 studies which were relevant to our case report^[3,5-15]. A PRISMA chart with the study selection process is outlined in Figure 3.

Result of literature review

The literature review showed that compartment syndrome varies with regards to its onset and implications after TKR surgery. The time period from TKR to fasciotomy ranged from 14 to 192 h (Table 1). Such variation may be attributed to the masking effect of spinal/epidural anaesthesia. Eight out of 25 patients who underwent fasciotomies had no complications. However, 15 patients developed complications 8 of whom had permanent

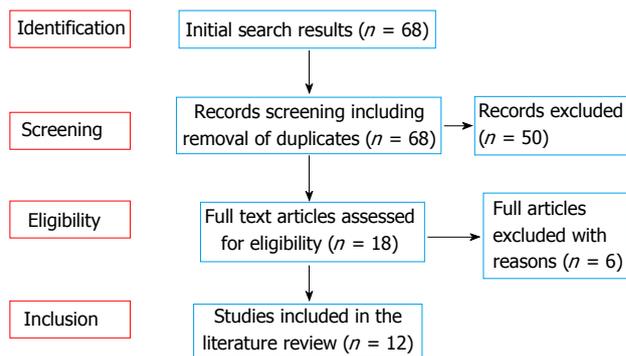


Figure 3 PRISMA chart of the study selection process.

foot drop; one patient underwent an above and another patient below knee amputation. It is therefore important to intervene in a timely fashion and have a low threshold of performing a fasciotomy to prevent such serious complications. On the other hand, a recent review of 6 cases of compartment syndrome post TKR surgery showed overall high complication rates associated with treatment in this group of patients^[3]. In particular, 2 patients developed periprosthetic infections one of whom ended up with an above knee amputation and 2 developed foot drops. As a result, authors suggested that surgeons need to maintain a relatively higher threshold for performing a fasciotomy following TKR in comparison to trauma patients who develop a compartment syndrome. However, it is worth mentioning that in this case series, all patients not only had a spinal anaesthetic but most of them also underwent vascular procedures prior to the fasciotomies. This may have adversely affected the result of the fasciotomies which were delayed in favour of such vascular interventions. In our case, had it not been for our low threshold for surgery and high index of suspicion, our patient may have developed complications. Therefore we disagree with the suggestion of delayed intervention in compartment syndrome developing after TKR surgery and support early treatment to avoid any complications.

DISCUSSION

Compartment syndrome following TKR is an exceptionally rare complication, with only a small number of cases documented in the literature^[3,5-15]. The commonest explanation is that a TKR involves the joint space without affecting the adjacent compartments^[6,7,15]. However there have been sporadic cases of compartment syndrome following TKR affecting the gluteal, thigh and leg compartments. The recommended treatment is urgent fasciotomy with subsequent debridement and wound closure.

Numerous factors contributing to the development of compartment syndrome and the delay in diagnosing it have been suggested in the literature as follows.

Tourniquet pressure

Tourniquet pressure has been highlighted as a potential cause of raised intracompartmental pressure due to

Table 1 Studies reporting compartment syndrome after total knee replacement

	Age	Tourniquet pressure (mmHg)	Anticoagulation	Anaesthetic	Time to treatment (h)	Location	Fasciotomy	Complications
Boonstra <i>et al</i> ^[5]	62	350	Yes	GA and Femoral block	24	Thigh	Yes	None
Haggis <i>et al</i> ^[6]	69	350	No	Epidural	14	Leg	Yes	Foot drop and equinus
	53	N/A	No	Epidural	38	Thigh	Yes	Foot drop and equinus
	65	300	No	Spinal	24	Leg	Yes	None
	48	350	No	Epidural	192	Leg	Yes	Foot drop and numb sole
	39	350	Yes	Epidural	20	Leg	Yes	Foot drop and equinus/ infected TKR
	49	350	No	Epidural	51	Leg	Yes	Foot drop
	61	350	Yes	Epidural	38	Leg	Yes	Below knee amputation
Hailer <i>et al</i> ^[7]	43	275	Yes	Epidural	50	Leg	Yes	Pes equinus. Complete plegia of all muscle groups distal to the knee. Anesthesia of the sole of the foot
Kort <i>et al</i> ^[8]	44	300	N/R	Spinal + Epidural	22	Leg	Yes	Neurologic impairment and pain
Kumar <i>et al</i> ^[9]	46	N/R	No	Spinal + Epidural	48	Gluteal	Yes	None
	72	N/R	Yes	Epidural	47	Gluteal	Yes	Trendelenburg gait
Lareau <i>et al</i> ^[10]	73	N/R	N/R	GA and Femoral block	Approximately 36	Thigh	Yes	None
Nadeem <i>et al</i> ^[11]	71	N/R	Yes	N/R	N/R	Thigh	Yes	None
Osteen <i>et al</i> ^[12]	52	N/R	N/R	Epidural	Approximately 48	Gluteal	Yes	None
Pacheco <i>et al</i> ^[13]	47	N/R	N/R	Epidural	44	Gluteal	Yes	Gluteal discomfort
	71	N/R	N/R	Epidural	Approximately 48	Gluteal	Yes	Motor and sensory impairment distal to the knee
Smith <i>et al</i> ^[14]	66	N/R	Yes	Epidural	N/R	Thigh	No	None
Tang <i>et al</i> ^[15]	62	300	N/R	Epidural	Approximately 48	Leg	Yes	Calf numbness
Vegari <i>et al</i> ^[3]	81	350	No	Spinal	20	Leg	Yes	Non-healing wounds
	74	325	No	Spinal + Epidural	24	Leg	Yes	Skin/muscle necrosis
	61	250	Yes	Spinal + Epidural	70	Leg	Yes	Foot drop
	56	300	Yes	Spinal + Epidural	17	Leg	Yes	None
	70	250	Yes	Spinal	18	Leg	Yes	Above knee amputation
	62	250	Yes	Spinal	26	Leg	Yes	Foot drop
Our case	72	300	Yes	Spinal + Epidural	31	Leg	Yes	None

N/R: Not recorded; N/A: Not applicable; GA: General anaesthesia; TKR: Total knee replacement.

reperfusion following tourniquet release^[8]. Haggis *et al*^[6] suggested a correlation between higher tourniquet pressure and long term complications with the patient having the lowest tourniquet pressure suffering no long term complications. However when holistically considering all the cases described; a correlation between tourniquet pressure and severity of long term complications could not be established (Table 1).

Anaesthesia

Epidural anaesthesia has been discussed in several case reports. Two studies^[7,15] described how a delay in the diagnosis of compartment syndrome due to the epidural masking pain, led to long term functional deficits. Two further studies^[9,13] found that symptoms of gluteal compartment syndrome in four patients following TKR only appeared after withdrawal of the epidural. Hence, Hailer *et al*^[7] suggested that epidural anaesthesia should be avoided after any lower limb orthopaedic surgery in order to allow for early detection of compartment syndrome.

Thromboprophylaxis

Despite papers suggesting that thromboprophylaxis may predispose to compartment syndrome due to associated excessive bleeding, only half of the cases presented in the literature received anticoagulant medication^[3,5-15].

Vascular injury

Vegari *et al*^[3] stated that vascular injury is the commonest cause of compartment syndrome following TKR. However, cases described in this review failed to determine any direct causal relationship.

Rehabilitation following surgery

Lareau *et al*^[10] suggested overuse of the continuous passive movement machine as a cause of compartment syndrome. Continuous flexion and extension of the knee joint for a prolonged period may decrease the volume of the compartments thereby increasing intra-compartmental pressure. Another case of compartment syndrome of the thigh following TKR reported that compartmental pressures (measured using a continuous intracompartmental

pressure monitor) would only increase on flexion of the knee joint^[14]. Knee flexion exacerbated the pain whilst increasing the compartmental pressures which confirms that pain is a very reliable indicator of the severity of compartment syndrome.

In the case presented hereby, we believe that a combination of using a tourniquet and maybe thromboprophylaxis were contributive factors for developing compartment syndrome. However, the use of regional anaesthetic certainly added to the delay in presenting the symptoms as well.

This case report and review of the literature emphasizes the importance of having a high index of suspicion and low threshold of intervention for compartment syndrome occurring after TKRs.

COMMENTS

Case characteristics

A 72-year-old presented with excruciating right lower leg pain one day following an elective total knee replacement.

Clinical diagnosis

Pain on passive movement of the toes, tension across the entirety of the calf as well as paraesthesia. The distal pulses in the leg were palpable but weak.

Differential diagnosis

Compartment syndrome vs simple postoperative swelling after total knee replacement (TKR) surgery.

Laboratory diagnosis

Not relevant in this case report. However, the Stryker Intra-Compartmental Pressure Monitor was used to measure intracompartmental pressures of the anterior, lateral and posterior compartments.

Treatment

Fasciotomy with decompression of all four leg compartments, followed by wound closure.

Related reports

Compartment syndrome following TKR is an exceptionally rare complication, with only a small number of cases documented in the literature. Factors potentially contributing to the development of compartment syndrome and the delay in its diagnosis include vascular injury, thromboprophylaxis, the use of a tourniquet and regional anaesthesia delaying the diagnosis.

Term explanation

Compartment syndrome is a serious condition that occurs due to elevation of interstitial pressure in closed fascial compartments resulting in microvascular compromise, myoneuronal function impairment and soft tissue necrosis.

Experiences and lessons

Compartment syndrome following TKR is rare. However, a high index of suspicion and low threshold of intervention is necessary in order to avoid disastrous consequences.

Peer-review

The authors presented a case with compartment syndrome following TKR, which was a rare complication successfully treated by urgent fasciotomy. The manuscript is well written.

REFERENCES

- 1 **Elliott KG**, Johnstone AJ. Diagnosing acute compartment syndrome. *J Bone Joint Surg Br* 2003; **85**: 625-632 [PMID: 12892179]
- 2 **Russell WL**, Apyan PM, Burns RP. Utilization and wide clinical implementation using the wick catheter for compartment pressure measurement. *Surg Gynecol Obstet* 1985; **160**: 207-210 [PMID: 3975792]
- 3 **Vegari DN**, Rangavajjula AV, Diiorio TM, Parvizi J. Fasciotomy following total knee arthroplasty: beware of terrible outcome. *J Arthroplasty* 2014; **29**: 355-359 [PMID: 23786987 DOI: 10.1016/j.arth.2013.05.013]
- 4 **Derrington MC**, Smith G. A review of studies of anaesthetic risk, morbidity and mortality. *Br J Anaesth* 1987; **59**: 815-833 [PMID: 3304374 DOI: 10.1093/bja/59.7.815]
- 5 **Boonstra RH**, Haverkamp D, Campo MM, van der Vis HM. Acute compartment syndrome of the thigh following total knee arthroplasty. *Knee* 2012; **19**: 151-153 [PMID: 21420301 DOI: 10.1016/j.knee.2011.02.007]
- 6 **Haggis P**, Yates P, Blakeway C, Fick D, Morgan DA, Holt M, Wood D. Compartment syndrome following total knee arthroplasty: a report of seven cases. *J Bone Joint Surg Br* 2006; **88**: 331-334 [PMID: 16498006 DOI: 10.1302/0301-620X.88B3.16919]
- 7 **Hailer NP**, Adalberth G, Nilsson OS. Compartment syndrome of the calf following total knee arthroplasty--a case report of a highly unusual complication. *Acta Orthop* 2007; **78**: 293-295 [PMID: 17464621 DOI: 10.1080/17453670710013825]
- 8 **Kort NP**, van Raay JJ, van Horn JR. Compartment syndrome and popliteal vascular injury complicating unicompartmental knee arthroplasty. *J Arthroplasty* 2007; **22**: 472-476 [PMID: 17400107 DOI: 10.1016/j.arth.2006.02.164]
- 9 **Kumar V**, Saeed K, Panagopoulos A, Parker PJ. Gluteal compartment syndrome following joint arthroplasty under epidural anaesthesia: a report of 4 cases. *J Orthop Surg (Hong Kong)* 2007; **15**: 113-117 [PMID: 17429132]
- 10 **Lareau JM**, Robbins CE, Talmo CT, Mehio AK, Puri L, Bono JV. Complications of femoral nerve blockade in total knee arthroplasty and strategies to reduce patient risk. *J Arthroplasty* 2012; **27**: 564-568 [PMID: 21908171 DOI: 10.1016/j.arth.2011.06.028]
- 11 **Nadeem RD**, Clift BA, Martindale JP, Hadden WA, Ritchie IK. Acute compartment syndrome of the thigh after joint replacement with anticoagulation. *J Bone Joint Surg Br* 1998; **80**: 866-868 [PMID: 9768900 DOI: 10.1302/0301-620X.80B5.8324]
- 12 **Osteen KD**, Haque SH. Bilateral gluteal compartment syndrome following right total knee revision: a case report. *Ochsner J* 2012; **12**: 141-144 [PMID: 22778678]
- 13 **Pacheco RJ**, Buckley S, Oxborrow NJ, Weeber AC, Allerton K. Gluteal compartment syndrome after total knee arthroplasty with epidural postoperative analgesia. *J Bone Joint Surg Br* 2001; **83**: 739-740 [PMID: 11476317 DOI: 10.1302/0301-620X.83B5.11763]
- 14 **Smith PN**, Rampersaud R, Rorabeck CH. Incipient compartment syndrome of the thigh following total knee arthroplasty. *J Arthroplasty* 1997; **12**: 835-838 [PMID: 9355016 DOI: 10.1016/S0883-5403(97)90017-6]
- 15 **Tang WM**, Chiu KY. Silent compartment syndrome complicating total knee arthroplasty: continuous epidural anesthesia masked the pain. *J Arthroplasty* 2000; **15**: 241-243 [PMID: 10708095 DOI: 10.1016/S0883-5403(00)90440-6]

P- Reviewer: Fenichel I, Ohishi T, Pastides PS, Zak L

S- Editor: Ji FF **L- Editor:** A **E- Editor:** Li D



Lateral subtalar dislocation: Case report and review of the literature

Ewout S Veltman, Ernst JA Steller, Philippe Wittich, Jort Keizer

Ewout S Veltman, Ernst JA Steller, Philippe Wittich, Jort Keizer, Department of Surgery, St. Antonius Ziekenhuis, 3435 CM Nieuwegein, the Netherlands

Author contributions: All authors contributed to the acquisition of data, drafting and revision of this manuscript.

Institutional review board statement: This case report and literature review was exempt from the Institutional Review Board standards at St. Antonius ziekenhuis Nieuwegein.

Informed consent statement: The patient involved in this study gave her verbal informed consent authorizing use and disclosure of her protected health information.

Conflict-of-interest statement: All the authors have no conflicts of interests to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Ewout S Veltman, MD, Department of Surgery, St. Antonius Ziekenhuis, Koekoekslaan 1, 3435 CM Nieuwegein, the Netherlands. wout.veltmann@gmail.com
Telephone: +31-88-3201925
Fax: +31-88-3206999

Received: April 28, 2016

Peer-review started: April 29, 2016

First decision: June 17, 2016

Revised: July 1, 2016

Accepted: July 14, 2016

Article in press: July 18, 2016

Published online: September 18, 2016

Abstract

A case of complicated lateral subtalar dislocation is presented and the literature concerning this injury is reviewed. Subtalar joint dislocations are rare and often the result of a high-energy trauma. Complications include avascular necrosis of the talus, infection, posttraumatic osteoarthritis requiring arthrodesis and chronic subtalar instability. Negative prognostic factors include lateral and complicated dislocations, total talar extrusions, and associated fractures. A literature search was performed to identify studies describing outcome after lateral subtalar joint dislocation. Eight studies including fifty patients could be included, thirty out of 50 patients suffered a complicated injury. Mean follow-up was fifty-five months. Ankle function was reported as good in all patients with closed lateral subtalar dislocation. Thirteen out of thirty patients with complicated lateral subtalar joint dislocation developed a complication. Avascular necrosis was present in nine patients with complicated injury. Four patients with complicated lateral subtalar dislocation suffered deep infection requiring treatment with antibiotics. In case of uncomplicated lateral subtalar joint dislocation, excellent functional outcome after closed reduction and immobilization can be expected. In case of complicated lateral subtalar joint dislocation immediate reduction, wound debridement and if necessary (external) stabilisation are critical. Up to fifty percent of patients suffering complicated injury are at risk of developing complications such as avascular talar necrosis and infection.

Key words: Trauma; Dislocation; Subtalar joint; Foot injury; Hindfoot surgery; External fixators

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Subtalar dislocations are a rare and severe injury which is often result of high-energy trauma. Sub-

talar dislocations represent 1%-2% of all dislocations. The foot is displaced laterally in about 25% of cases. Excellent outcome can be expected in patients with uncomplicated lateral subtalar dislocation if immediate closed reduction is achieved. In case of complicated subtalar joint dislocations requiring open reduction, wound debridement, appropriate joint reduction and additional stabilisation with an external fixation are critical. A complication rate up to 50% can be expected in these patients.

Veltman ES, Steller EJA, Wittich P, Keizer J. Lateral subtalar dislocation: Case report and review of the literature. *World J Orthop* 2016; 7(9): 623-627 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i9/623.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i9.623>

INTRODUCTION

Subtalar joint dislocation is defined as a simultaneous dislocation of the subtalar (talocalcaneal) and talonavicular joint^[1]. Subtalar dislocations are rare and often the result of high-energy trauma^[1,2]. Rarity of this injury can be attributed to the presence of strong ligaments connecting the talus and the calcaneus, the strong biomechanical properties of the ankle and the tight joint capsule^[2]. The trauma causing this type of injury is frequently a fall from considerable height or a motor vehicle accident^[4]. In American literature, a large number of patients feature trauma after jumps during a basketball game, which has led to the term "basketball foot"^[3,4].

Subtalar joint dislocations are frequently accompanied by fractures of the adjacent tarsal and metatarsal bones. Severe soft tissue injury can also be present^[1]. The currently used classification of subtalar dislocations was introduced by Broca in 1853 and adjusted by Malgaigne *et al*^[5] in 1856. Dislocations of the talus are classified based on the direction in which the foot is dislocated^[1,6]. In about 72% of patient the talus is dislocated medially, lateral dislocation is present in 26% of patients and posterior or anterior dislocation in the remainder of patients^[1]. Lateral subtalar joint dislocations are produced by forced eversion with the foot in dorsiflexion^[1]. Inability to reduce lateral subtalar dislocations can be caused by interposition of the posterior tibialis tendon in case of rupture of the flexor retinaculum^[7,8]. Pure ligamentous dislocations have an excellent prognosis after proper reduction^[9]. Diagnosing additional injury is essential, as fractures of the lateral talar process and the sustentaculum tali may lead to the rapid development of posttraumatic osteoarthritis of the subtalar joint^[10]. Talar avascular necrosis is reported in up to 50% of patients after complicated lateral subtalar dislocation^[11].

Isolated lateral subtalar joint dislocation has only scarcely been described in literature. We report the case of a patient suffering complicated lateral subtalar joint dislocation and we give a comprehensive review of the

available literature on lateral subtalar joint dislocations.

CASE REPORT

In May 2015, a 31-year-old male was presented to the emergency room with pain of the foot after eversion trauma while jumping on a trampoline. Initial trauma screening revealed a hemodynamically stable patient with a complicated (Gustilo type 3) subtalar joint dislocation of the right leg (Figure 1). During trauma screening no other injuries were detected. The patient was transported to the OR within 4 h of presentation. The dislocated talus was immediately reduced using a surgical spoon and a femoral head impactor. We performed meticulous wound debridement, after which the wound was closed transcutaneously over a subcutaneous low vacuum drain. A joint bridging external fixator was constructed with additional kirschner-wires for reduction and temporary stabilisation (Figure 2). A postoperative computed tomography (CT) scan showed several small fracture fragments of the talar bone with congruent ankle and subtalar joints. There were no fractures of the adjacent tarsal and metatarsal bones.

The medial wound healed uneventfully. Eight weeks postoperatively the external fixator and kirschner wires were removed during a visit at the outpatient clinic. At this time the patient engaged in physical therapy and commenced bearing full weight on the affected leg. One year after injury the patient is walking without pain, only using a cane for long distances. Range of motion of the ankle is not restricted (Figure 3). Conventional radiographs show early signs of talar avascular necrosis (Figure 4), without associated clinical symptoms.

Review of the literature

Methods: The search was limited to humans aged over eighteen years with a subtalar dislocation. PubMed/MEDLINE, EMBASE, and the Cochrane Library were searched from up to April 1st 2016. Exclusion criteria were minor age and subtalar dislocation in medial, anterior or posterior direction. Case reports were excluded to limit report bias. The lists of references of retrieved publications were manually checked for additional studies potentially meeting the inclusion criteria and not found by the electronic search. Studies reporting various types of subtalar dislocation were identified and only included if the results of patients with lateral subtalar dislocation could be extracted separately.

We collected all information regarding the level of evidence, baseline patient characteristics, baseline clinical findings and mean period of follow-up. Data regarding type and timing of surgery, postoperative regimen, complications, functional outcome, radiological outcome and patient satisfaction were extracted.

Results: The literature search displayed 367 studies, of which eight studies including fifty patients could be included^[6,11-17]. General characteristics can be found in Table 1. All reported numbers are sample-size weighted.

Table 1 General characteristics

Ref.	Year	No. of patients	Follow-up (mo)	Age	Male	Female	Left	Right	Complicated injury	Avascular necrosis	Infection
Camarda <i>et al</i> ^[12]	2015	3	69	50	x	x	x	x	0	0	0
Edmunds <i>et al</i> ^[13]	1991	4	36	43	4	0	3	1	4	3	1
Garofalo <i>et al</i> ^[14]	2004	5	122	32	4	1	3	2	4	0	0
Goldner <i>et al</i> ^[11]	1995	10	36	26	8	2	x	x	10	5	2
Jungbluth <i>et al</i> ^[6]	2010	6	58	42	4	2	x	x	2	0	0
Karampinas <i>et al</i> ^[15]	2009	9	21	32	7	2	4	5	9	1	1
Merchan <i>et al</i> ^[16]	1992	10	66	36	7	3	2	8	1	0	0
Ruhmann <i>et al</i> ^[17]	2016	3	84	39	3	0	2	1	0	0	0
Total/mean		50	55	34	37	10	14	17	30	9	4



Figure 1 Initial trauma screening revealed a hemodynamically stable patient with a complicated (Gustilo type 3) subtalar joint dislocation of the right leg. A and B: Gustilo grade 3 complicated lateral dislocation of the right foot; C: Radiograph showing lateral dislocation of the subtalar joint.



Figure 2 The wound is closed primarily after meticulous debridement and an external fixator is applied.

Eighty-seven percent of patients were male. Mean age was thirty-four years. Subtalar dislocations were evenly distributed over the left and right extremity. Thirty out of 50 patients suffered a complicated injury. Unfortunately Gustilo grading of complicated injury was not reported in all studies and therefore not available for analysis in this study. Associated fractures of the tarsal or metatarsal bones were present in seventeen patients, posterior tibial tendon rupture was present in six patients.

Closed lateral subtalar dislocations were treated with reduction and below the knee casting. Closed reduction was successful in all of these cases. All complicated lateral subtalar dislocations were treated with wound debridement. Additional fixation with k-wires was per-

formed in three patients. An external fixator was placed in eleven patients, the other nineteen patients were treated with a below the knee cast. The patients were non-weight bearing for a mean period of seven weeks (range 4-12), after which the cast was removed and patients were allowed to bear weight. Mean follow-up was fifty-five months. Four studies^[6,12,15,17] provide patient reported outcome with the use of the American Orthopaedic Foot and Ankle Society score (AOFAS)^[18], which has not been validated for this purpose. Mean AOFAS score at follow-up was 82. Ankle function was reported as good in all patients with closed lateral subtalar dislocation. Severe pain was reported in nine patients with avascular necrosis and in two additional patients with severe osteoarthritis.

Radiologic assessment revealed subtalar osteoarthritis (Altman *et al*^[19] type 2 or 3) in eight out of fifty patients. Avascular necrosis was present in nine additional patients. Patients with avascular necrosis were eventually treated with arthrodesis of the ankle in most cases. Four patients with complicated lateral subtalar dislocation suffered deep infection requiring treatment with antibiotics.

DISCUSSION

Lateral subtalar joint dislocation is a rare and severe injury. The number of patients reported with this type of injury is therefore small. The high-energy trauma which is needed to cause lateral dislocation is reflected in the percentage of patients with severe soft tissue damage.



Figure 3 Excellent ankle function is restored at final follow-up (A and B).



Figure 4 Radiograph of the ankle at follow-up, showing early signs of avascular talar necrosis.

Immediate reduction, extensive wound debridement and when necessary additional stabilisation are key features of treatment and should be performed as short after presentation as possible.

Complications are not evenly distributed among patients with closed and complicated injury. The literature review reports avascular necrosis or deep infection in 13 out of 30 patients with complicated lateral subtalar dislocation, compared to no avascular necrosis or deep infection in twenty patients with closed subtalar dislocation. Complicated injury is the main predictor of poor outcome. Avascular necrosis or deep infection can be expected in about 50% of cases.

In all cases, in addition to plain ankle and foot radiographs, a CT-scan should be performed after reduction to document additional bony injury to the subtalar area and adjacent bones. Additional injury is often underestimated in a plain radiograph of the hindfoot, but can have serious consequences such as osteoarthritis or chronic instability if undetected.

The duration of immobilization remains controversial. In uncomplicated injury an early weight-bearing protocol seems possible, after a lower leg cast for a period of 3-4 wk. In case of complicated injury or instability the use of an external fixator might be necessary, prohibiting patients from walking for a period of 6-12 wk depending on the extent of additional fractures of the tarsal and metatarsal bones.

This study gives a comprehensive review of the literature concerning lateral subtalar joint dislocation, treatment and expected outcome. Unfortunately, our literature search shows a lack of quality evidence. High level evidence on treatment and prognosis of subtalar joint dislocations is absent due to the rarity of this injury. The weaknesses of the original studies are reflected in our results. Patient specific characteristics such as smoking, obesity and diabetes, which affect the risk of developing avascular necrosis or infection, were not reported in the original studies and therefore not analysed. Daily practice would benefit from a large scale prospective study on optimal treatment, however with the extremely low number of patients suffering this injury this can be qualified as wishful thinking.

Excellent outcome can be expected in patients with uncomplicated lateral subtalar dislocation if immediate closed reduction is achieved. In case of complicated subtalar joint dislocations requiring open reduction, wound debridement, appropriate joint reduction and additional stabilisation with an external fixation are critical. A complication rate up to 50% can be expected in these patients. The review helps physicians treating a patient with a lateral subtalar dislocation to discuss treatment and prognosis of this severe injury of the foot.

COMMENTS

Case characteristics

Hindfoot pain and Gustilo grade 3 complicated injury of the hindfoot after jumping the trampoline.

Clinical diagnosis

Gustilo grade 3 complicated, isolated lateral subtalar joint dislocation.

Differential diagnosis

Ankle luxation fracture, talar fracture, talar extrusion, talar fracture, calcaneal fracture.

Laboratory diagnosis

All labs were within normal limits.

Imaging diagnosis

Plain radiographs (before reduction) of the foot showed a lateral subtalar

dislocation. A post-reduction computed tomography-scan demonstrated multiple small fracture fragments of the talar bone, without fractures of the adjacent bones.

Treatment

Immediate reduction, wound debridement and external fixation.

Related reports

See reference list for more articles on the same subject.

Experiences and lessons

Immediate reduction and meticulous wound debridement are key features in treating subtalar dislocations. In case of instability external fixation can be applied.

Peer-review

A simple rare article with simple to understand and something to learn.

REFERENCES

- 1 **Hoexum F**, Heetveld MJ. Subtalar dislocation: two cases requiring surgery and a literature review of the last 25 years. *Arch Orthop Trauma Surg* 2014; **134**: 1237-1249 [PMID: 24993588 DOI: 10.1007/s00402-014-2040-6]
- 2 **Giannoulis D**, Papadopoulos DV, Lykissas MG, Koulouvaris P, Gkiatas I, Mavrodontidis A. Subtalar dislocation without associated fractures: Case report and review of literature. *World J Orthop* 2015; **6**: 374-379 [PMID: 25893182 DOI: 10.5312/wjo.v6.i3.374]
- 3 **Simon LC**, Schulz AP, Faschingbauer M, Morlock M, Jürgens C. ["Basketball Foot"--long-time prognosis after peritalar dislocation]. *Sportverletz Sportschaden* 2008; **22**: 31-37 [PMID: 18350482 DOI: 10.1055/s-2008-1027208]
- 4 **Wagner R**, Blattert TR, Weckbach A. Talar dislocations. *Injury* 2004; **35** Suppl 2: SB36-SB45 [PMID: 15315877 DOI: 10.1016/j.injury.2004.07.010]
- 5 **Malgaigne JF**, Buerger CG. Die Knochenbrüche und Verrekungen. Stuttgart: Rieger, 1856
- 6 **Jungbluth P**, Wild M, Hakimi M, Gehrman S, Djuricic M, Windolf J, Muhr G, Källicke T. Isolated subtalar dislocation. *J Bone Joint Surg Am* 2010; **92**: 890-894 [PMID: 20360512 DOI: 10.2106/JBJS.I.00490]
- 7 **Waldrop J**, Ebraheim NA, Shapiro P, Jackson WT. Anatomical considerations of posterior tibialis tendon entrapment in irreducible lateral subtalar dislocation. *Foot Ankle* 1992; **13**: 458-461 [PMID: 1483606 DOI: 10.1177/107110079201300805]
- 8 **de Palma L**, Santucci A, Marinelli M, Borgogno E, Catalani A. Clinical outcome of closed isolated subtalar dislocations. *Arch Orthop Trauma Surg* 2008; **128**: 593-598 [PMID: 17909825 DOI: 10.1007/s00402-007-0459-8]
- 9 **Rammelt S**, Goronzy J. Subtalar dislocations. *Foot Ankle Clin* 2015; **20**: 253-264 [PMID: 26043242 DOI: 10.1016/j.fcl.2015.02.008]
- 10 **Bibbo C**, Lin SS, Abidi N, Berberian W, Grossman M, Gebauer G, Behrens FF. Missed and associated injuries after subtalar dislocation: the role of CT. *Foot Ankle Int* 2001; **22**: 324-328 [PMID: 11354446]
- 11 **Goldner JL**, Poletti SC, Gates HS, Richardson WJ. Severe open subtalar dislocations. Long-term results. *J Bone Joint Surg Am* 1995; **77**: 1075-1079 [PMID: 7608231]
- 12 **Camarda L**, Abruzzese A, La Gattuta A, Lentini R, D'Arienzo M. Results of closed subtalar dislocations. *Musculoskelet Surg* 2016; **100**: 63-69 [PMID: 26254192 DOI: 10.1007/s12306-015-0380-1]
- 13 **Edmunds I**, Elliott D, Nade S. Open subtalar dislocation. *Aust N Z J Surg* 1991; **61**: 681-686 [PMID: 1877937 DOI: 10.1111/j.1445-2197.1991.tb00320.x]
- 14 **Garofalo R**, Moretti B, Ortolano V, Cariola P, Solarino G, Wettstein M, Mouhsine E. Peritalar dislocations: a retrospective study of 18 cases. *J Foot Ankle Surg* 2004; **43**: 166-172 [PMID: 15181433 DOI: 10.1053/j.jfas.2004.03.008]
- 15 **Karampinas PK**, Kavroudakis E, Polyzois V, Vlamis J, Pneumaticos S. Open talar dislocations without associated fractures. *Foot Ankle Surg* 2014; **20**: 100-104 [PMID: 24796827 DOI: 10.1016/j.jfas.2013.12.005]
- 16 **Merchan EC**. Subtalar dislocations: long-term follow-up of 39 cases. *Injury* 1992; **23**: 97-100 [PMID: 1572724 DOI: 10.1016/0020-1383(92)90041-P]
- 17 **Ruhmann F**, Poujardieu C, Vernois J, Gayet LE. Isolated Acute Traumatic Subtalar Dislocations: Review of 13 Cases at a Mean Follow-Up of 6 Years and Literature Review. *J Foot Ankle Surg* 2016 [PMID: 26947001 DOI: 10.1053/j.jfas.2016.01.044]
- 18 **Kitaoka HB**, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. *Foot Ankle Int* 1994; **15**: 349-353 [PMID: 7951968 DOI: 10.1177/107110079401500701]
- 19 **Altman RD**, Hochberg M, Murphy WA, Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995; **3** Suppl A: 3-70 [PMID: 8581752]

P- Reviewer: Brasileiro B, Wani IA

S- Editor: Ji FF L- Editor: A E- Editor: Li D





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 October 18; 7(10): 628-699



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 329 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), **Cyprus (1)**, Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (17), and United States (65).

EDITOR-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

ASSOCIATE EDITOR

Wasim S Khan, *London*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tai chung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarn, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Tai chung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Moraes Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*
Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Bao-Gan Peng, *Beijing*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srecko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*

Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efsthios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiyah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*
 Keith Baldwin, *Philadelphia*

Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort Sam Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

REVIEW

- 628 Skeletal muscle mitochondrial health and spinal cord injury
O'Brien LC, Gorgey AS
- 638 Magnetic resonance imaging after anterior cruciate ligament reconstruction: A practical guide
Grassi A, Bailey JR, Signorelli C, Carbone G, Tchonang Wakam A, Lucidi GA, Zaffagnini S

MINIREVIEWS

- 650 Treatment of the ulnar nerve for overhead throwing athletes undergoing ulnar collateral ligament reconstruction
Conti MS, Camp CL, Elattrache NS, Altchek DW, Dines JS
- 657 Posterior ankle impingement syndrome: A systematic four-stage approach
Yasui Y, Hannon CP, Hurley E, Kennedy JG

ORIGINAL ARTICLE

Retrospective Cohort Study

- 664 Effect of body mass index on functional outcome in primary total knee arthroplasty - a single institution analysis of 2180 primary total knee replacements
O'Neill SC, Butler JS, Daly A, Lui DF, Kenny P

Retrospective Study

- 670 Outcome of repair of chronic tear of the pectoralis major using corkscrew suture anchors by box suture sliding technique
Joshi D, Jain JK, Chaudhary D, Singh U, Jain V, Lal A

Observational Study

- 678 Is there a weekend effect in hip fracture patients presenting to a United Kingdom teaching hospital?
Mathews JA, Vindlacherivu M, Khanduja V

Randomized Controlled Trial

- 687 Volar locking distal radius plates show better short-term results than other treatment options: A prospective randomised controlled trial
Drobotz H, Koval L, Weninger P, Luscombe R, Jeffries P, Ehrendorfer S, Heal C

CASE REPORT

- 695 Laminar screw fixation in the subaxial cervical spine: A report on three cases
Tanabe H, Aota Y, Saito T

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Aditya Vikram Maheshwari, MD, Assistant Professor, Department of Orthopaedics, SUNY Downstate Medical Center, Brooklyn, NY 11203, United States

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthritis, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central, and Scopus.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Xin Kong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL BOARD MEMBERS
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
 Xiu-Xia Song, Director
 Fang-Fang Ji, Vice Director
World Journal of Orthopedics
 Baishideng Publishing Group Inc
 8226 Regency Drive, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLICATION DATE
 October 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>

Skeletal muscle mitochondrial health and spinal cord injury

Laura C O'Brien, Ashraf S Gorgey

Laura C O'Brien, Ashraf S Gorgey, Spinal Cord Injury and Disorders Service, Hunter Holmes McGuire VA Medical Center, Richmond, VA 23249, United States

Laura C O'Brien, Department of Physiology and Biophysics, Virginia Commonwealth University, Richmond, VA 23298, United States

Ashraf S Gorgey, Department of Physical Medicine and Rehabilitation, Virginia Commonwealth University, Richmond, VA 23298, United States

Author contributions: O'Brien LC and Gorgey AS wrote the paper.

Conflict-of-interest statement: The authors declare no conflict of interest.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Ashraf S Gorgey, MPT, PhD, FACSM, Chief of Spinal Cord Injury Research, Spinal Cord Injury and Disorders Service, Hunter Holmes McGuire VA Medical Center, 1201 Broad Rock Blvd, Richmond, VA 23249, United States. ashraf.gorgey@va.gov
Telephone: +1-804-6755000
Fax: +1-804-6755223

Received: May 5, 2016

Peer-review started: May 9, 2016

First decision: June 13, 2016

Revised: June 18, 2016

Accepted: August 15, 2016

Article in press: August 16, 2016

Published online: October 18, 2016

Abstract

Mitochondria are the main source of cellular energy production and are dynamic organelles that undergo biogenesis, remodeling, and degradation. Mitochondrial dysfunction is observed in a number of disease states including acute and chronic central or peripheral nervous system injury by traumatic brain injury, spinal cord injury (SCI), and neurodegenerative disease as well as in metabolic disturbances such as insulin resistance, type II diabetes and obesity. Mitochondrial dysfunction is most commonly observed in high energy requiring tissues like the brain and skeletal muscle. In persons with chronic SCI, changes to skeletal muscle may include remarkable atrophy and conversion of muscle fiber type from oxidative to fast glycolytic, combined with increased infiltration of intramuscular adipose tissue. These changes contribute to a proinflammatory environment, glucose intolerance and insulin resistance. The loss of metabolically active muscle combined with inactivity predisposes individuals with SCI to type II diabetes and obesity. The contribution of skeletal muscle mitochondrial density and electron transport chain activity to the development of the aforementioned comorbidities following SCI is unclear. A better understanding of the mechanisms involved in skeletal muscle mitochondrial dynamics is imperative to designing and testing effective treatments for this growing population. The current editorial will review ways to study mitochondrial function and the importance of improving skeletal muscle mitochondrial health in clinical populations with a special focus on chronic SCI.

Key words: Mitochondria; Spinal cord injuries; Body composition; Diabetes mellitus; Obesity; Metabolism

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Mitochondria are the main source of cellular energy production and have decreased function in many disease states. After spinal cord injury (SCI) there is a dramatic deterioration of body composition including

increased adipose tissue deposition, skeletal muscle atrophy and conversion from oxidative to glycolytic skeletal muscle fibers. These changes put persons with SCI at a high risk for developing cardiovascular disease and type II diabetes. How skeletal muscle mitochondrial function is impacted after human SCI has yet to be determined. The current editorial will discuss the importance of studying skeletal muscle mitochondrial function after SCI.

O'Brien LC, Gorgey AS. Skeletal muscle mitochondrial health and spinal cord injury. *World J Orthop* 2016; 7(10): 628-637 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/628.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.628>

INTRODUCTION

Mitochondria produce over 95% of ATP through the process of oxidative phosphorylation. Under physiological conditions, mitochondria undergo a dynamic process of biogenesis, remodeling and degradation. Dysregulation of this balance results in decreased energy production, increased reactive oxygen species (ROS) and in some cases cell death. Mitochondrial dysfunction is observed with normal aging, as well as in many disease states. It is well established that damage to the central nervous system (CNS) by traumatic brain injury, spinal cord injury (SCI) and neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis) is associated with mitochondrial dysfunction^[1]. Recent studies have suggested that metabolic disorders including atherosclerosis, hypertension, cancer, insulin resistance, type II diabetes and obesity is associated with decreased mitochondrial function as well^[2-4]. A better understanding of the mechanisms involved in mitochondrial dynamics and ways to improve mitochondrial health could be important for designing and testing effective treatments for these clinical populations. In this editorial we will discuss the importance of studying skeletal muscle mitochondrial health and function in persons with chronic SCI.

SCI is a devastating medical condition that results from direct or indirect damage to the spinal cord. This damage can be caused by trauma or by several pathological conditions. There are approximately 12000 new cases of SCI each year in the United States and nearly half of these individuals are between the ages of 16 and 30^[5]. Because of the near-normal life expectancy of persons with SCI, the estimated lifetime cost of health care and living expenses for a person with a cervical SCI is over \$3 million, not including lost income^[5]. After SCI, patients undergo severe body composition deterioration and skeletal muscle changes that predispose them to metabolic disorders like type II diabetes and cardiovascular disease^[6-8].

MITOCHONDRIAL DYNAMICS AND ENERGY PRODUCTION

Cellular energy production

Mitochondria are double membraned organelles. The outer mitochondrial membrane (OMM) allows the passage of small molecules through voltage-dependent anion channels; however, access to the inner mitochondrial membrane (IMM) is much more tightly regulated^[9]. The electron transport chain (ETC) consists of IMM-bound protein complexes I -IV and functions to maintain the electrochemical gradient across the IMM that is necessary to make ATP^[10] (Figures 1 and 2). This electrochemical gradient is achieved by the pumping of protons (H⁺) from the mitochondrial matrix into the intermembrane space (IMS) by complexes I, III, and IV (Figure 2). Disruption of this gradient results in decreased ATP synthesis and causes electrons to leak from the ETC and react with molecular oxygen in the matrix to create the ROS superoxide (O₂⁻)^[11].

The main source of electrons for the ETC is the reduced form of nicotinamide adenine dinucleotide (NADH) produced by the citric acid (Kreb's) cycle and the oxidation of fatty acids (β -oxidation; Figure 1). Another source of electrons is succinate, a byproduct of the Kreb's cycle. Electrons enter the ETC through complex I (NADH dehydrogenase) or complex II (succinate dehydrogenase) and are then transferred to complex III (cytochrome bc1 complex) through a lipid soluble carrier molecule, coenzyme Q (Figure 2). Electrons then move between complex III and IV by way of a water soluble carrier molecule, cytochrome c. Molecular oxygen is reduced and water is produced by complex IV, cytochrome c oxidase. The movement of electrons through the ETC is coupled to ATP production by ATP synthase, or complex V. This protein complex converts ADP to ATP and is coupled to proton movement from the IMS back into the matrix. This process of synthesizing ATP in the mitochondria is called oxidative phosphorylation.

Electrons can leak from the ETC and react with molecular oxygen to create ROS like O₂⁻ (Figure 2). Complex I and III are the primary sites of electron leak and are sensitive to ROS injury^[11]. ROS play an important role in skeletal muscle plasticity and activate many signaling cascades including increasing peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 α), the master regulator of mitochondrial biogenesis^[12,13]. Cells have antioxidants in the cytoplasm and mitochondrial matrix in order to neutralize ROS. However, if the balance between antioxidants and ROS is disturbed, large amounts of ROS can result in the oxidation of proteins, lipids and DNA. As discussed above, access across the IMM is tightly regulated and disruption of the electrochemical gradient across it results in decreased ATP synthesis and increased ROS production. In addition to mitochondrial ROS production, in skeletal muscle, superoxide is also produced

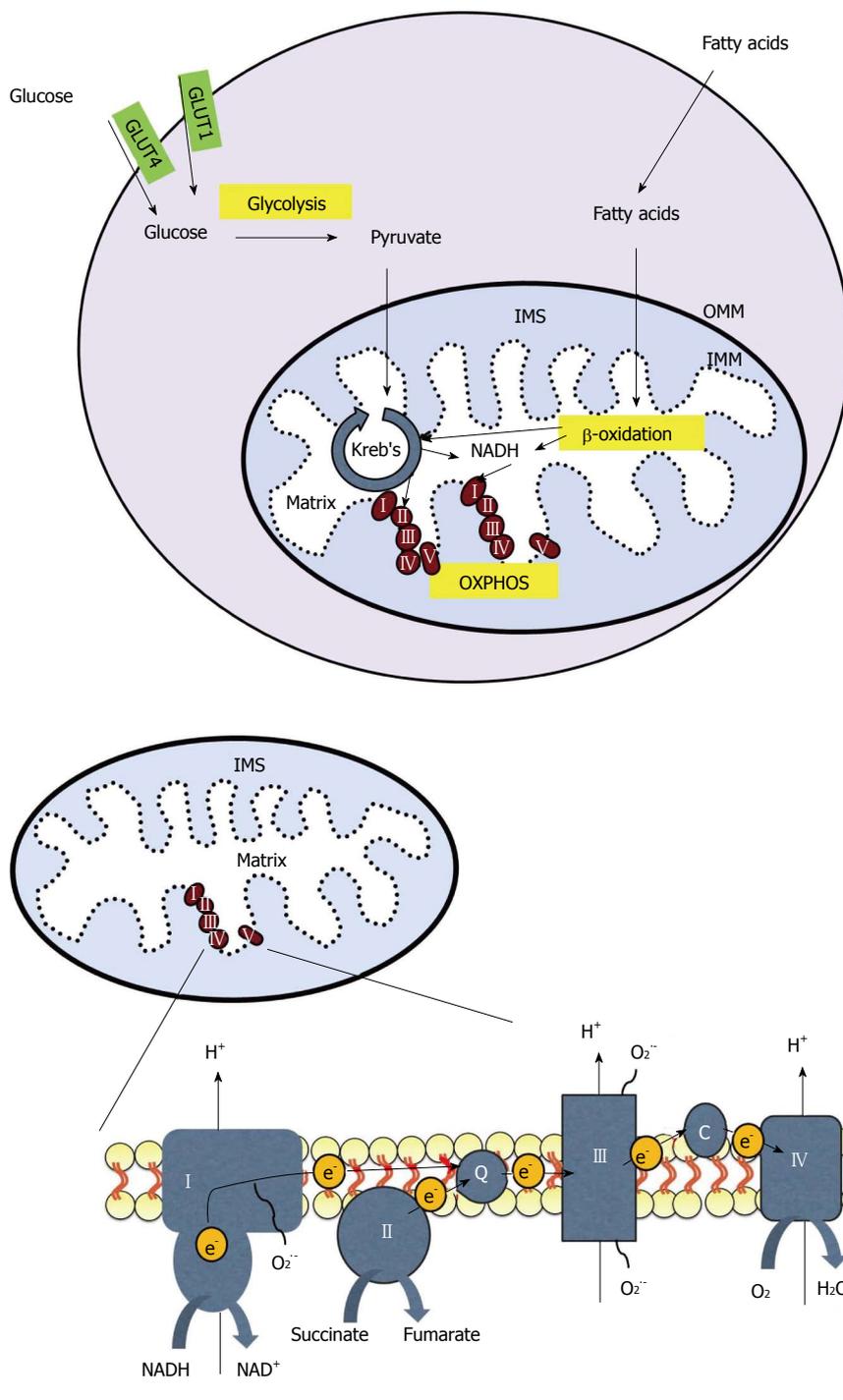


Figure 1 Cellular energy production. In skeletal muscle, glucose enters the cell through glucose transporter type 1 or 4 (GLUT1 or GLUT4, respectively). Glucose is converted to pyruvate in the glycolysis pathway. Pyruvate is transported across the outer and inner mitochondrial membranes (OMM and IMM, respectively) and into the mitochondrial matrix where it is converted into acetyl-coA. Fatty acids undergo β -oxidation in the mitochondria, creating acetyl-coA and NADH. Acetyl-coA is utilized by the Krebs cycle, creating NADH and succinate which enter the electron transport chain (ETC) at complex I and II, respectively. The movement of electrons through the ETC is coupled to the production of ATP in a process called OXPHOS. IMS: Intermembrane space; OXPHOS: Oxidative phosphorylation.

Figure 2 The electron transport chain is located on the inner mitochondrial membrane. Electrons (e^-) enter through complex I or II and are transferred to complex III by coenzyme Q (Q). Electrons then move between complex III and IV by cytochrome c (c). Electrons can leak from the chain and react with oxygen to create superoxide (O_2^-). The movement of electrons is coupled to the pumping of protons (H^+) from the mitochondrial matrix into the intermembrane space (IMS). This gradient is then used by ATP synthase, or complex V, to generate ATP.

in the sarcoplasmic reticulum, transverse tubules, sarcolemma, and the cytosol^[14].

Mitochondrial biogenesis

Mitochondrial biogenesis includes transcription of genes by the nuclear and mitochondrial genomes. Mitochondrial DNA (mtDNA) is circular and encodes 13 proteins

essential for ETC function. MtDNA is susceptible to damage by ROS because it is not protected by histones like nuclear DNA. Deletions in mtDNA are observed in several diseases and may result in a decrease in gene expression of mitochondrial encoded genes important for ETC function, resulting in increased ROS production and decreased ATP production.

Mitochondrial biogenesis is regulated, in part, by the master regulator PGC-1 α and varies based on the energy needs of the cell. After translation and mitochondrial import, proteins of the ETC are assembled into protein complexes and generate ATP through oxidative phosphorylation^[13].

Mitochondrial dynamics

Remodeling of mitochondria occurs by fission and fusion. Fusion of mitochondria results in a large mitochondrial network, while fission pinches off a part of this network. After fission, mitochondrial fragments can be tagged for degradation by a specialized type of autophagy, termed mitophagy, or they can rejoin the mitochondrial network by fusion. When there is a scarcity of nutrients the mitochondrial network is fused in order to increase mitochondrial bioenergetic efficiency, while an abundance of nutrients results in a fragmented mitochondrial network^[15]. Mitochondria also make contact with other subcellular organelles, including the endoplasmic reticulum. These endoplasmic reticulum mitochondria-associated membranes play an important role in cellular functions including mitochondrial division, apoptosis, and lipid and calcium regulation^[15,16].

METHODS FOR STUDYING MITOCHONDRIA

There are multiple techniques that can be used to measure mitochondrial dynamics and function. These include measuring mRNA or protein expression, enzyme activity, and oxygen consumption by respirometry. Skeletal muscle biopsies are most commonly used in human studies since spinal cord and brain tissue is inaccessible.

mRNA and protein expression

mRNA and protein expression of molecules involved in mitochondrial biogenesis, remodeling and degradation can be observed by quantitative (real-time) polymerase chain reaction (qPCR) and western blot. This is the easiest way to detect changes in cellular signaling cascades and allows for the elucidation of where in the cascade there is a potential defect caused by disease or injury. Western blot analysis of ETC proteins and other mitochondrial proteins can be assayed as an estimate of respiratory chain function and mitochondrial mass, respectively. However, this type of analysis assumes that the proteins will then be imported into the mitochondria and properly assembled into the ETC complexes. There is also the assumption that a change in the expression of one protein from each complex is representative of the whole complex when in fact there are multiple proteins in each complex. For example, the mammalian complex I contains 45 different proteins^[17].

Enzyme activity

One way to estimate mitochondrial function is to measure the activity of individual ETC complexes using a spectro-

photometer. This can be done by measuring specific donor-acceptor oxidoreductase activities as previously described^[18,19]. By using specific substrates and inhibitors each complex can be assayed individually. Linked activity between complexes can be measured by adding either NADH (for complex I) or succinate (for complex II) and measuring the reduction of cytochrome c by complex III^[18,19]. Other key enzymes of the citric acid cycle (*i.e.*, citrate synthase) and β -oxidation pathways [*i.e.*, β -hydroxyacyl-CoA dehydrogenase (β -HAD)] can also be measured spectrophotometrically^[18,20].

The benefit of spectrophotometric analysis is that it uses a small amount of tissue, samples can be previously frozen, and spectrophotometers are common lab equipment^[19]. A limitation of spectrophotometric analysis is that it shows maximum capacity of individual complexes and does not necessarily represent physiological function. However, with the limited sample size obtained by human skeletal muscle biopsy and the need by many labs to freeze tissue, this may be a good option for many research groups.

Previous research has used human biopsy or autopsy specimens from tissues such as skeletal muscle, liver and skin^[21]. Studies have been conducted using both tissue homogenates and isolated mitochondria from previously frozen human skeletal muscle^[22,23]. Isolating mitochondria is ideal for understanding mechanism; however, the cellular context is lost. Also, more tissue is needed compared to running tissue homogenates because some mitochondria will be lost in the isolation process. A benefit of analyzing tissue homogenates is that the mitochondria remain in their cellular context, giving a more physiological reading. A limitation of analyzing tissue homogenates is the high non-mitochondrial NADH oxidase activity of some tissues^[24].

Respirometry

Measuring oxygen consumption of isolated mitochondria or permeabilized cells by respirometry is currently the gold standard for assaying mitochondrial function. Respiration shows that the ETC is functioning because oxygen is necessary for ATP synthesis. The addition of substrates and inhibitors allows assessment of individual ETC complexes and coupling to ATP synthesis. Respiration can determine mitochondrial dysfunction not identified by spectrophotometric analysis, including impairment in mitochondrial membrane transport, problems with substrate utilization, and defects in fatty acid metabolism^[25]. Protocols have recently been developed to analyze mitochondrial function from as little as 20-50 mg of muscle tissue^[26]. However, this technique is labor intensive and samples cannot be previously frozen because freezing uncouples the ETC from ATP synthesis.

CHANGES IN BODY COMPOSITION AND METABOLISM AFTER SCI

SCI is usually a result of trauma to the spine, resulting

in damage to cells that send messages to and from the brain. Damage can be to the upper motor neurons that project from the brain to the spinal cord or lower motor neurons that project from the spinal cord to the muscles. The location and severity of the injury largely determines the extent of impairment. Injuries resulting in motor and sensory impairment distal to the level of injury are classified as either complete or incomplete SCI, with incomplete injury resulting in spared sensation and/or motor function. The loss of peripheral nervous system control below the level of injury results in decreased mobility. This immobility, combined with hormonal changes and poor dietary habits result in decreased muscle mass and increased adipose deposition^[6,7,27]. These changes put individuals with SCI at a high risk for developing cardiovascular disease, type II diabetes, and obesity^[7,28,29]. Recent studies have shown a link between the deterioration in body composition and the impaired metabolic profile after SCI^[30,31]. However, there are still many questions that remain unanswered at the cellular level.

Body composition after SCI

Drastic changes in body composition follow SCI^[8]. Skeletal muscle atrophy combined with inactivity and poor diet contributes to the increased prevalence of obesity in this population^[32]. Excess body fat, particularly around the waist, is a risk factor for a number of conditions including cardiovascular and metabolic disease^[31,33]. Measurements of body mass index (BMI) do not take into account regional distribution of adipose tissue and underestimate fat mass in persons with SCI^[34]. Waist circumference measurements do not distinguish between subcutaneous adipose tissue and ectopic [visceral adipose tissue (VAT)]. It is important to distinguish between these two adipose tissue types, as an increase in VAT is a risk factor for cardiovascular and metabolic disease^[35]. Waist circumference measurements underestimate the amount of VAT in individuals with SCI. Increased waist circumference is correlated with the amount of VAT in able bodied (AB) individuals but this is not the case in the SCI population^[36]. SCI individuals have more VAT than AB individuals with the same waist circumference^[37]. Collectively, these data suggest that there adipose tissue deposition is increased after SCI and that the distribution is altered compared to AB individuals. For a review on this topic, see^[8].

In addition to increased adipose tissue disposition, individuals with SCI experience significant changes to their skeletal muscle. These changes include significant muscle atrophy, conversion of muscle fiber type from oxidative to fast glycolytic, and an increase in intramuscular fat (IMF). Both complete and incomplete SCI results in substantial atrophy of muscles below the level of injury. Incomplete SCI resulted in a 33% decrease in thigh muscle cross sectional area and an increase in IMF six weeks post-injury compared to AB controls^[32]. The conversion of muscle fiber type to fast glycolytic results in an quickly fatigued

muscle that can be damaged easily^[38]. Additionally, an increase in fast glycolytic muscle fibers decreases insulin sensitivity and may lead to diabetes^[39].

As discussed above, increased VAT, but not subcutaneous adipose tissue, is a risk factor for cardiovascular disease, glucose intolerance, insulin resistance, and hyperlipidemia^[35]. This may be due to the infiltration of immune cells into VAT and subsequent secretion of inflammatory cytokines including tumor necrosis factor α (TNF α), interleukin-1 β (IL-1 β) and IL-6. Previous research suggests that inflammatory cytokines released by adipose tissue accelerate skeletal muscle atrophy^[40-42]. A recent study investigating the interactions between adipose tissue and skeletal muscle revealed that VAT adipocytes from obese subjects decreased cultured myotube thickness and resulted in a gene expression profile suggestive of muscle atrophy^[41]. The proposed mechanism is through the release of IL-1 β and IL-6 and decreased insulin growth factor signaling, resulting in insulin resistance. Another type of adipose tissue that is similar to VAT, IMF, is increased after SCI and may be a contributing factor to the development of insulin resistance^[32,43]. The mechanisms underlying the interplay between adipose tissue and skeletal muscle are just beginning to be understood.

Metabolism after SCI

In addition to changes in body composition, metabolism is disrupted after SCI. As many as 55% of individuals with SCI have metabolic syndrome, which is characterized by three or more of the following conditions: Obesity, high blood pressure, insulin resistance, high triglycerides, and low high-density lipoprotein (HDL) cholesterol levels^[44]. Impaired glucose tolerance was observed in 56% of persons with SCI, compared with only 18% of AB controls^[45]. Individuals with SCI also have increased low-density lipoprotein (LDL) cholesterol^[46,47]. These conditions worsen with age and put individuals at risk for developing cardiovascular disease and type II diabetes.

MITOCHONDRIAL HEALTH STATUS

AFTER SCI

CNS mitochondrial health after SCI

The immediate damage to the spinal cord, including damage to axons and cells at the injury site is called primary injury. Models of SCI have shown an increase in intracellular sodium, chloride and calcium 15-60 min after injury^[48]. An increase in intracellular calcium may result in apoptosis if the excess calcium taken up by mitochondria triggers mitochondrial permeability transition pore opening. Following this initial insult is a secondary injury, characterized by invasion of inflammatory cells and more cell death as cells invade not only the injury site, but also the spared nervous tissue. Neuronal death leads to loss of motor or sensory function and loss of oligodendrocytes leads to axonal demyelination^[49].

Mitochondrial respiration in the spinal cord through

complexes I and II is decreased and oxidative stress is increased at 12 and 24 h, but not after 6 h after SCI in a rat model^[50]. In another study respiration and complex I and IV enzyme activity was decreased in the spinal cord after SCI^[51]. In this study mitochondrial function was improved by treatment with an antioxidant. Complex I, complex IV, and pyruvate dehydrogenase are mitochondrial enzymes that are particularly vulnerable to damage by ROS and are decreased after SCI^[52]. Decreasing ROS or increasing function of these enzymes may improve functional outcomes after SCI.

Skeletal muscle mitochondrial health after SCI

There is limited knowledge about the changes in mitochondrial function following SCI in humans. However, indirect evidence of mitochondrial function using near-infrared resonance spectroscopy to measure tissue oxygenation revealed that muscle oxidative capacity was decreased 50%-60% in participants with SCI 2.7-22 years after injury compared to AB controls^[53]. A similar deficit was observed using histochemistry to measure succinate dehydrogenase (SDH) activity in muscle biopsy samples from paralyzed muscle 2-11 years post injury compared to AB controls^[54,55]. In contrast, a study analyzing SDH and GAPDH activity, markers of complex II and glycolytic capacity, respectively, 6-24 wk after injury found increased activity despite greater fatigability of muscles^[38]. The reason for these discrepant results is unclear, but it could be that early after injury muscle atrophy and fiber type changes results in a compensatory increase in oxidative and glycolytic enzymes but long periods of muscle inactivity result in reduced activity of oxidative and glycolytic pathways^[38,54,55]. More research is needed to determine the effect of SCI on mitochondrial function.

Mitochondria are also dysfunctional in a number of metabolic diseases including type II diabetes and obesity. A large network of fused mitochondria is observed in healthy skeletal muscle, while muscle from obese and type II diabetics is fragmented^[56]. Skeletal muscle mitochondrial function is decreased as well, with a 2-3 fold decrease in NADH oxidase (complex I) activity normalized to mitochondrial content in obese and type II diabetics compared to control^[57].

Exercise interventions have been shown to increase skeletal muscle mitochondrial function and improve insulin sensitivity in obesity, diabetes, and aging^[58,59]. Some options for exercise intervention after SCI include neuromuscular electrical stimulation-induced weight lifting and functional electrical stimulation (FES) cycling. Sixteen weeks of electrical stimulation-induced resistance training increased muscle mass and improved mitochondrial function by 25% in patients with SCI^[60]. FES cycling has also been shown to increase mitochondrial function in patients with SCI. Eight weeks of FES cycling resulted in an increase in citrate synthase, a marker of mitochondrial mass^[61]. Similarly, studies found increased citrate synthase as well as increased function of enzymes involved in

glycolysis and β -oxidation^[62,63]. Finally, SDH was increased after 4 wk of training, suggesting that complex II activity is increased with exercise^[64]. Similarly, a recent study showed that a single session of low frequency electrical stimulation increased genes involved in muscle metabolism, including PGC-1 α ^[65]. Collectively, these studies suggest that paralyzed skeletal muscle is malleable and can increase mitochondrial function in response to exercise. Additionally, IMF has been shown to decrease after resistance exercise training^[66]. This would provide additional benefit to skeletal muscle and may improve insulin sensitivity.

SIGNIFICANCE AND FUTURE

DIRECTIONS

Mitochondria are vital for energy production and play a role in a number of cellular processes including cell signaling, cell cycle progression, calcium regulation and cell death. These organelles are dynamic, and undergo changes in activity and number in response to cellular energy needs. A decrease in neuron and skeletal muscle mitochondrial function is observed in a number of disease and injury states including CNS trauma, neurodegenerative disease, type II diabetes and obesity^[1-3]. However, we know very little about mitochondrial function in patients with chronic SCI. We are just beginning to understand the role of mitochondria in insulin resistance and how skeletal muscle mitochondrial function is disrupted in patients with SCI. Future research needs to be done using functional assays to assess activity of individual ETC complexes, as well as its coupling to ATP synthesis.

Increasing mitochondrial function by pharmacological activation of mitochondrial biogenesis is an active area of research^[67]. There are a number of FDA approved medications as well as naturally occurring substances that activate mitochondrial biogenesis. For example, resveratrol, which is found in red wine, activates sirtuin 1 (SIRT1) and increases PGC-1 α activity and mitochondrial function and was shown to improve insulin resistance in diabetic patients^[68,69]. Small molecules that activate SIRT1 with improved bioavailability and potency have been developed and are currently being tested in humans. FDA approved pharmacological activators of mitochondrial biogenesis include the β_2 -adrenergic receptor agonist formoterol^[70], the anti-diabetic drug metformin^[71], the phosphodiesterase inhibitor sildenafil^[72], the PPAR γ agonist rosiglitazone^[73], the mitochondrial permeability transition pore inhibitor cyclosporine A^[74], and the angiotensin-converting enzyme inhibitor captopril^[75], among others. Although these compounds are thought to exert their effects at least in part by increasing mitochondrial biogenesis, there are currently no specific activators of mitochondrial biogenesis. Future studies need to investigate the safety and efficacy of systemically increasing mitochondrial biogenesis, as well as optimizing dosing in order to maximize the therapeutic benefit.

In order to study mitochondrial function after disease

or injury or to assess the efficacy of mitochondrial targeted therapies, skeletal muscle biopsies could be used because of the inaccessibility of the brain and spinal cord in humans. However, recent studies have suggested that the bioenergetic profile of blood cells is associated with physical function and inflammation as well^[76,77]. Indeed, mitochondrial dysfunction is seen in blood from patients with a number of diseases including neurodegenerative diseases and type II diabetes^[78,79]. Peripheral blood mononuclear cells from patients with type II diabetes and chronic kidney disease have increased inflammatory cytokines, decreased mitochondrial function and increased ROS production^[80]. These studies suggest that blood cell bioenergetics may predict systemic mitochondrial function and may act as biomarkers for metabolic stress and surrogate markers for the severity of disease progression and the efficacy of therapeutics^[80,81]. This represents an intriguing possibility, as obtaining blood samples are much less invasive than biopsies and could be taken more frequently in order to better characterize the time course of therapeutic intervention.

There are a number of different techniques for analyzing cellular signaling pathways and mitochondrial function. Researchers should carefully weigh the convenience of non-invasive techniques with the mechanistic detail provided by analyzing biopsy tissue. If choosing to analyze biopsy tissue, care should be taken to obtain the proper amount of tissue required for the assay and to prepare it properly in order to preserve mitochondrial function. For samples that need to be frozen, spectrophotometric analysis may be the best option for analyzing mitochondrial function, while respiration will be ideal for fresh tissue samples. Another research consideration is whether or not to isolate mitochondria and this may depend on the sample size.

As discussed above, both resistance training and FES cycling has been shown to increase mitochondrial function in persons with SCI. In addition, electrical stimulation-induced resistance training reduced VAT and IMF and increased insulin sensitivity while increasing muscle mass^[66]. FES cycling has been shown to improve insulin sensitivity as well, but the effect on muscle size and body composition were minimal to modest^[82]. It is unknown if conditioning the muscles with resistance training prior to FES cycling would result in greater mitochondrial and metabolic outcomes.

CONCLUSION

There is limited knowledge regarding skeletal muscle mitochondrial health following SCI. Challenges may stem from difficulties in capturing muscle biopsies and running biochemical analysis to determine mitochondrial mass or activity by spectroscopy or respiration. Non-invasive procedures like near-infrared resonance spectroscopy may reflect mitochondrial activity; however, mechanistic dysfunctions individual of complexes may be limited.

A better understanding of how mitochondrial function

is impacted in patients with chronic SCI is critical for developing interventions to increase mitochondrial function and improve metabolic outcomes. Skeletal muscle or blood cell bioenergetics may predict overall mitochondrial health and therefore be a surrogate marker of disease progression and treatment efficacy. Increasing mitochondrial function immediately following SCI may decrease cell death and improve functional outcomes. Improvement in mitochondrial function by exercise or pharmacological interventions in chronic SCI may decrease comorbidities. This will result in better health for patients and a lower financial burden for their health care. A better understanding of mitochondrial biology may also translate to a number of other diseases in which mitochondrial are dysfunctional, particularly insulin resistance, type II diabetes, and obesity.

ACKNOWLEDGMENTS

We would like to thank the Hunter Holmes McGuire VA Medical Center and Virginia Commonwealth University for providing the environment to conduct clinical research.

REFERENCES

- 1 **Itoh K**, Nakamura K, Iijima M, Sesaki H. Mitochondrial dynamics in neurodegeneration. *Trends Cell Biol* 2013; **23**: 64-71 [PMID: 23159640 DOI: 10.1016/j.tcb.2012.10.006]
- 2 **Chan DC**. Mitochondria: dynamic organelles in disease, aging, and development. *Cell* 2006; **125**: 1241-1252 [PMID: 16814712 DOI: 10.1016/j.cell.2006.06.010]
- 3 **Zhao J**, Zhang J, Yu M, Xie Y, Huang Y, Wolff DW, Abel PW, Tu Y. Mitochondrial dynamics regulates migration and invasion of breast cancer cells. *Oncogene* 2013; **32**: 4814-4824 [PMID: 23128392 DOI: 10.1038/onc.2012.494]
- 4 **Phielix E**, Mensink M. Type 2 diabetes mellitus and skeletal muscle metabolic function. *Physiol Behav* 2008; **94**: 252-258 [PMID: 18342897 DOI: 10.1016/j.physbeh.2008.01.020]
- 5 **National Spinal Cord Injury Statistical Center**. Spinal cord injury facts and figures at a glance. *J Spinal Cord Med* 2013; **36**: 1-2 [PMID: 23433327 DOI: 10.1179/1079026813Z.000000000136]
- 6 **Kocina P**. Body composition of spinal cord injured adults. *Sports Med* 1997; **23**: 48-60 [PMID: 9017859]
- 7 **Gater DR**. Obesity after spinal cord injury. *Phys Med Rehabil Clin N Am* 2007; **18**: 333-351, vii [PMID: 17543776 DOI: 10.1016/j.pmr.2007.03.004]
- 8 **Gorgey AS**, Dolbow DR, Dolbow JD, Khalil RK, Castillo C, Gater DR. Effects of spinal cord injury on body composition and metabolic profile - part I. *J Spinal Cord Med* 2014; **37**: 693-702 [PMID: 25001559 DOI: 10.1179/2045772314Y.00000000245]
- 9 **Lemasters JJ**, Holmuhamedov E. Voltage-dependent anion channel (VDAC) as mitochondrial governor--thinking outside the box. *Biochim Biophys Acta* 2006; **1762**: 181-190 [PMID: 16307870 DOI: 10.1016/j.bbadis.2005.10.006]
- 10 **Saraste M**. Oxidative phosphorylation at the fin de siècle. *Science* 1999; **283**: 1488-1493 [PMID: 10066163]
- 11 **Turrens JF**. Mitochondrial formation of reactive oxygen species. *J Physiol* 2003; **552**: 335-344 [PMID: 14561818 DOI: 10.1113/jphysiol.2003.049478]
- 12 **Hoppeler H**, Baum O, Lurman G, Mueller M. Molecular mechanisms of muscle plasticity with exercise. *Compr Physiol* 2011; **1**: 1383-1412 [PMID: 23733647 DOI: 10.1002/cphy.c100042]
- 13 **Scarpulla RC**, Vega RB, Kelly DP. Transcriptional integration of mitochondrial biogenesis. *Trends Endocrinol Metab* 2012; **23**: 459-466 [PMID: 22817841 DOI: 10.1016/j.tem.2012.06.006]

- 14 **Powers SK**, Ji LL, Kavazis AN, Jackson MJ. Reactive oxygen species: impact on skeletal muscle. *Compr Physiol* 2011; **1**: 941-969 [PMID: 23737208 DOI: 10.1002/cphy.c100054]
- 15 **Schrepfer E**, Scorrano L. Mitofusins, from Mitochondria to Metabolism. *Mol Cell* 2016; **61**: 683-694 [PMID: 26942673 DOI: 10.1016/j.molcel.2016.02.022]
- 16 **Vance JE**. MAM (mitochondria-associated membranes) in mammalian cells: lipids and beyond. *Biochim Biophys Acta* 2014; **1841**: 595-609 [PMID: 24316057 DOI: 10.1016/j.bbali.2013.11.014]
- 17 **Carroll J**, Fearnley IM, Skehel JM, Shannon RJ, Hirst J, Walker JE. Bovine complex I is a complex of 45 different subunits. *J Biol Chem* 2006; **281**: 32724-32727 [PMID: 16950771 DOI: 10.1074/jbc.M607135200]
- 18 **Brass EP**, Hiatt WR, Gardner AW, Hoppel CL. Decreased NADH dehydrogenase and ubiquinol-cytochrome c oxidoreductase in peripheral arterial disease. *Am J Physiol Heart Circ Physiol* 2001; **280**: H603-H609 [PMID: 11158957]
- 19 **Spinazzi M**, Casarin A, Pertegato V, Salviati L, Angelini C. Assessment of mitochondrial respiratory chain enzymatic activities on tissues and cultured cells. *Nat Protoc* 2012; **7**: 1235-1246 [PMID: 22653162 DOI: 10.1038/nprot.2012.058]
- 20 **Morash AJ**, Kotwica AO, Murray AJ. Tissue-specific changes in fatty acid oxidation in hypoxic heart and skeletal muscle. *Am J Physiol Regul Integr Comp Physiol* 2013; **305**: R534-R541 [PMID: 23785078 DOI: 10.1152/ajpregu.00510.2012]
- 21 **Hoppel CL**, Kerr DS, Dahms B, Roessmann U. Deficiency of the reduced nicotinamide adenine dinucleotide dehydrogenase component of complex I of mitochondrial electron transport. Fatal infantile lactic acidosis and hypermetabolism with skeletal-cardiac myopathy and encephalopathy. *J Clin Invest* 1987; **80**: 71-77 [PMID: 3110216 DOI: 10.1172/JCI113066]
- 22 **Kelly NA**, Ford MP, Standaert DG, Watts RL, Bickel CS, Moellering DR, Tuggle SC, Williams JY, Lieb L, Windham ST, Bamman MM. Novel, high-intensity exercise prescription improves muscle mass, mitochondrial function, and physical capacity in individuals with Parkinson's disease. *J Appl Physiol* (1985) 2014; **116**: 582-592 [PMID: 24408997 DOI: 10.1152/jappphysiol.01277.2013]
- 23 **Menshikova EV**, Ritov VB, Fairfull L, Ferrell RE, Kelley DE, Goodpaster BH. Effects of exercise on mitochondrial content and function in aging human skeletal muscle. *J Gerontol A Biol Sci Med Sci* 2006; **61**: 534-540 [PMID: 16799133]
- 24 **Trounce IA**, Kim YL, Jun AS, Wallace DC. Assessment of mitochondrial oxidative phosphorylation in patient muscle biopsies, lymphoblasts, and transmittochondrial cell lines. *Methods Enzymol* 1996; **264**: 484-509 [PMID: 8965721]
- 25 **Puchowicz MA**, Varnes ME, Cohen BH, Friedman NR, Kerr DS, Hoppel CL. Oxidative phosphorylation analysis: assessing the integrated functional activity of human skeletal muscle mitochondria-case studies. *Mitochondrion* 2004; **4**: 377-385 [PMID: 16120399 DOI: 10.1016/j.mito.2004.07.004]
- 26 **Bharadwaj MS**, Tyrrell DJ, Lyles MF, Demons JL, Rogers GW, Molina AJ. Preparation and respirometric assessment of mitochondria isolated from skeletal muscle tissue obtained by percutaneous needle biopsy. *J Vis Exp* 2015; Epub ahead of print [PMID: 25741892 DOI: 10.3791/52350]
- 27 **Bauman WA**, Spungen AM. Metabolic changes in persons after spinal cord injury. *Phys Med Rehabil Clin N Am* 2000; **11**: 109-140 [PMID: 10680161]
- 28 **Duckworth WC**, Solomon SS, Jallepalli P, Heckemeyer C, Finnern J, Powers A. Glucose intolerance due to insulin resistance in patients with spinal cord injuries. *Diabetes* 1980; **29**: 906-910 [PMID: 7429029]
- 29 **Lavela SL**, Weaver FM, Goldstein B, Chen K, Miskevics S, Rajan S, Gater DR. Diabetes mellitus in individuals with spinal cord injury or disorder. *J Spinal Cord Med* 2006; **29**: 387-395 [PMID: 17044389]
- 30 **Gorgey AS**, Gater DR. Regional and relative adiposity patterns in relation to carbohydrate and lipid metabolism in men with spinal cord injury. *Appl Physiol Nutr Metab* 2011; **36**: 107-114 [PMID: 21326384 DOI: 10.1139/H10-091]
- 31 **Gorgey AS**, Mather KJ, Gater DR. Central adiposity associations to carbohydrate and lipid metabolism in individuals with complete motor spinal cord injury. *Metabolism* 2011; **60**: 843-851 [PMID: 20870252 DOI: 10.1016/j.metabol.2010.08.002]
- 32 **Gorgey AS**, Dudley GA. Skeletal muscle atrophy and increased intramuscular fat after incomplete spinal cord injury. *Spinal Cord* 2007; **45**: 304-309 [PMID: 16940987 DOI: 10.1038/sj.sc.3101968]
- 33 **Nakamura T**, Tokunaga K, Shimomura I, Nishida M, Yoshida S, Kotani K, Islam AH, Keno Y, Kobatake T, Nagai Y. Contribution of visceral fat accumulation to the development of coronary artery disease in non-obese men. *Atherosclerosis* 1994; **107**: 239-246 [PMID: 7980698]
- 34 **Spungen AM**, Adkins RH, Stewart CA, Wang J, Pierson RN, Waters RL, Bauman WA. Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. *J Appl Physiol* (1985) 2003; **95**: 2398-2407 [PMID: 12909613 DOI: 10.1152/jappphysiol.00729.2002]
- 35 **Jensen MD**. Role of body fat distribution and the metabolic complications of obesity. *J Clin Endocrinol Metab* 2008; **93**: S57-S63 [PMID: 18987271 DOI: 10.1210/jc.2008-1585]
- 36 **Gorgey AS**, Mather KJ, Poarch HJ, Gater DR. Influence of motor complete spinal cord injury on visceral and subcutaneous adipose tissue measured by multi-axial magnetic resonance imaging. *J Spinal Cord Med* 2011; **34**: 99-109 [PMID: 21528633 DOI: 10.1179/107902610X12911165975106]
- 37 **Edwards LA**, Bugaresti JM, Buchholz AC. Visceral adipose tissue and the ratio of visceral to subcutaneous adipose tissue are greater in adults with than in those without spinal cord injury, despite matching waist circumferences. *Am J Clin Nutr* 2008; **87**: 600-607 [PMID: 18326597]
- 38 **Castro MJ**, Apple DF, Staron RS, Campos GE, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* (1985) 1999; **86**: 350-358 [PMID: 9887150]
- 39 **Simoneau JA**, Kelley DE. Altered glycolytic and oxidative capacities of skeletal muscle contribute to insulin resistance in NIDDM. *J Appl Physiol* (1985) 1997; **83**: 166-171 [PMID: 9216960]
- 40 **Hoppeler H**. Molecular networks in skeletal muscle plasticity. *J Exp Biol* 2016; **219**: 205-213 [PMID: 26792332 DOI: 10.1242/jeb.128207]
- 41 **Pellegrinelli V**, Rouault C, Rodriguez-Cuenca S, Albert V, Edom-Vovard F, Vidal-Puig A, Clément K, Butler-Browne GS, Lacasa D. Human Adipocytes Induce Inflammation and Atrophy in Muscle Cells During Obesity. *Diabetes* 2015; **64**: 3121-3134 [PMID: 25695947 DOI: 10.2337/db14-0796]
- 42 **Kelley DE**, Goodpaster BH. Stewing in Not-So-Good Juices: Interactions of Skeletal Muscle With Adipose Secretions. *Diabetes* 2015; **64**: 3055-3057 [PMID: 26294424 DOI: 10.2337/db15-0403]
- 43 **Elder CP**, Apple DF, Bickel CS, Meyer RA, Dudley GA. Intramuscular fat and glucose tolerance after spinal cord injury—a cross-sectional study. *Spinal Cord* 2004; **42**: 711-716 [PMID: 15303112 DOI: 10.1038/sj.sc.3101652]
- 44 **Nelson MD**, Widman LM, Abresch RT, Stanhope K, Havel PJ, Styne DM, McDonald CM. Metabolic syndrome in adolescents with spinal cord dysfunction. *J Spinal Cord Med* 2007; **30** Suppl 1: S127-S139 [PMID: 17874698]
- 45 **Bauman WA**, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. *Metabolism* 1994; **43**: 749-756 [PMID: 8201966]
- 46 **Nash MS**, Mendez AJ. A guideline-driven assessment of need for cardiovascular disease risk intervention in persons with chronic paraplegia. *Arch Phys Med Rehabil* 2007; **88**: 751-757 [PMID: 17532897 DOI: 10.1016/j.apmr.2007.02.031]
- 47 **Bauman WA**, Spungen AM, Zhong YG, Rothstein JL, Petry C, Gordon SK. Depressed serum high density lipoprotein cholesterol levels in veterans with spinal cord injury. *Paraplegia* 1992; **30**: 697-703 [PMID: 1448297 DOI: 10.1038/sc.1992.136]
- 48 **LoPachin RM**, Gaughan CL, Lehning EJ, Kaneko Y, Kelly TM, Blight A. Experimental spinal cord injury: spatiotemporal characterization of elemental concentrations and water contents in axons and neuroglia. *J Neurophysiol* 1999; **82**: 2143-2153 [PMID:

- 10561394]
- 49 **Rabchevsky AG**, Patel SP, Springer JE. Pharmacological interventions for spinal cord injury: where do we stand? How might we step forward? *Pharmacol Ther* 2011; **132**: 15-29 [PMID: 21605594 DOI: 10.1016/j.pharmthera.2011.05.001]
 - 50 **Sullivan PG**, Krishnamurthy S, Patel SP, Pandya JD, Rabchevsky AG. Temporal characterization of mitochondrial bioenergetics after spinal cord injury. *J Neurotrauma* 2007; **24**: 991-999 [PMID: 17600515 DOI: 10.1089/neu.2006.0242]
 - 51 **Patel SP**, Sullivan PG, Pandya JD, Goldstein GA, VanRooyen JL, Yonutas HM, Eldahan KC, Morehouse J, Magnuson DS, Rabchevsky AG. N-acetylcysteine amide preserves mitochondrial bioenergetics and improves functional recovery following spinal trauma. *Exp Neurol* 2014; **257**: 95-105 [PMID: 24805071 DOI: 10.1016/j.expn.eurol.2014.04.026]
 - 52 **McEwen ML**, Sullivan PG, Rabchevsky AG, Springer JE. Targeting mitochondrial function for the treatment of acute spinal cord injury. *Neurotherapeutics* 2011; **8**: 168-179 [PMID: 21360236 DOI: 10.1007/s13311-011-0031-7]
 - 53 **Ericksen ML**, Ryan TE, Young HJ, McCully KK. Near-infrared assessments of skeletal muscle oxidative capacity in persons with spinal cord injury. *Eur J Appl Physiol* 2013; **113**: 2275-2283 [PMID: 23703066 DOI: 10.1007/s00421-013-2657-0]
 - 54 **Martin TP**, Stein RB, Hoepfner PH, Reid DC. Influence of electrical stimulation on the morphological and metabolic properties of paralyzed muscle. *J Appl Physiol* (1985) 1992; **72**: 1401-1406 [PMID: 1534322]
 - 55 **Grimby G**, Broberg C, Krotkiewska I, Krotkiewski M. Muscle fiber composition in patients with traumatic cord lesion. *Scand J Rehabil Med* 1976; **8**: 37-42 [PMID: 132700]
 - 56 **Kelley DE**, He J, Menshikova EV, Ritov VB. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. *Diabetes* 2002; **51**: 2944-2950 [PMID: 12351431]
 - 57 **Ritov VB**, Menshikova EV, Azuma K, Wood R, Toledo FG, Goodpaster BH, Ruderman NB, Kelley DE. Deficiency of electron transport chain in human skeletal muscle mitochondria in type 2 diabetes mellitus and obesity. *Am J Physiol Endocrinol Metab* 2010; **298**: E49-E58 [PMID: 19887598 DOI: 10.1152/ajpendo.00317.2009]
 - 58 **Toledo FG**, Goodpaster BH. The role of weight loss and exercise in correcting skeletal muscle mitochondrial abnormalities in obesity, diabetes and aging. *Mol Cell Endocrinol* 2013; **379**: 30-34 [PMID: 23792186 DOI: 10.1016/j.mce.2013.06.018]
 - 59 **Lanza IR**, Nair KS. Muscle mitochondrial changes with aging and exercise. *Am J Clin Nutr* 2009; **89**: 467S-471S [PMID: 19056588 DOI: 10.3945/ajcn.2008.26717D]
 - 60 **Ryan TE**, Brizendine JT, Backus D, McCully KK. Electrically induced resistance training in individuals with motor complete spinal cord injury. *Arch Phys Med Rehabil* 2013; **94**: 2166-2173 [PMID: 23816921 DOI: 10.1016/j.apmr.2013.06.016]
 - 61 **Chilibeck PD**, Bell G, Jeon J, Weiss CB, Murdoch G, MacLean I, Ryan E, Burnham R. Functional electrical stimulation exercise increases GLUT-1 and GLUT-4 in paralyzed skeletal muscle. *Metabolism* 1999; **48**: 1409-1413 [PMID: 10582549]
 - 62 **Kjaer M**, Mohr T, Biering-Sørensen F, Bangsbo J. Muscle enzyme adaptation to training and tapering-off in spinal-cord-injured humans. *Eur J Appl Physiol* 2001; **84**: 482-486 [PMID: 11417439]
 - 63 **Crameri RM**, Weston A, Climstein M, Davis GM, Sutton JR. Effects of electrical stimulation-induced leg training on skeletal muscle adaptability in spinal cord injury. *Scand J Med Sci Sports* 2002; **12**: 316-322 [PMID: 12383078]
 - 64 **Rochester L**, Barron MJ, Chandler CS, Sutton RA, Miller S, Johnson MA. Influence of electrical stimulation of the tibialis anterior muscle in paraplegic subjects. 2. Morphological and histochemical properties. *Paraplegia* 1995; **33**: 514-522 [PMID: 8524604 DOI: 10.1038/sc.1995.112]
 - 65 **Petrie M**, Suneja M, Shields RK. Low-frequency stimulation regulates metabolic gene expression in paralyzed muscle. *J Appl Physiol* (1985) 2015; **118**: 723-731 [PMID: 25635001 DOI: 10.1152/jappphysiol.00628.2014]
 - 66 **Gorgy AS**, Mather KJ, Cupp HR, Gater DR. Effects of resistance training on adiposity and metabolism after spinal cord injury. *Med Sci Sports Exerc* 2012; **44**: 165-174 [PMID: 21659900 DOI: 10.1249/MSS.0b013e31822672aa]
 - 67 **Whitaker RM**, Corum D, Beeson CC, Schnellmann RG. Mitochondrial Biogenesis as a Pharmacological Target: A New Approach to Acute and Chronic Diseases. *Annu Rev Pharmacol Toxicol* 2016; **56**: 229-249 [PMID: 26566156 DOI: 10.1146/annurev-pharmtox-010715-103155]
 - 68 **Lagouge M**, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F, Messadeq N, Milne J, Lambert P, Elliott P, Geny B, Laakso M, Puigserver P, Auwerx J. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1 α . *Cell* 2006; **127**: 1109-1122 [PMID: 17112576 DOI: 10.1016/j.cell.2006.11.013]
 - 69 **Brasnyó P**, Molnár GA, Mohás M, Markó L, Laczy B, Cseh J, Mikolás E, Szijártó IA, Mérei A, Halmi R, Mészáros LG, Sümegi B, Wittmann I. Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients. *Br J Nutr* 2011; **106**: 383-389 [PMID: 21385509 DOI: 10.1017/S0007114511000316]
 - 70 **Wills LP**, Trager RE, Beeson GC, Lindsey CC, Peterson YK, Beeson CC, Schnellmann RG. The β 2-adrenoceptor agonist formoterol stimulates mitochondrial biogenesis. *J Pharmacol Exp Ther* 2012; **342**: 106-118 [PMID: 22490378 DOI: 10.1124/jpet.112.191528]
 - 71 **Kukidome D**, Nishikawa T, Sonoda K, Imoto K, Fujisawa K, Yano M, Motoshima H, Taguchi T, Matsumura T, Araki E. Activation of AMP-activated protein kinase reduces hyperglycemia-induced mitochondrial reactive oxygen species production and promotes mitochondrial biogenesis in human umbilical vein endothelial cells. *Diabetes* 2006; **55**: 120-127 [PMID: 16380484]
 - 72 **Whitaker RM**, Wills LP, Stallons LJ, Schnellmann RG. cGMP-selective phosphodiesterase inhibitors stimulate mitochondrial biogenesis and promote recovery from acute kidney injury. *J Pharmacol Exp Ther* 2013; **347**: 626-634 [PMID: 24042162 DOI: 10.1124/jpet.113.208017]
 - 73 **Pardo R**, Enguix N, Lasheras J, Feliu JE, Kralli A, Villena JA. Rosiglitazone-induced mitochondrial biogenesis in white adipose tissue is independent of peroxisome proliferator-activated receptor γ coactivator-1 α . *PLoS One* 2011; **6**: e26989 [PMID: 22087241 DOI: 10.1371/journal.pone.0026989]
 - 74 **Osman MM**, Lulic D, Glover L, Stahl CE, Lau T, van Loveren H, Borlongan CV. Cyclosporine-A as a neuroprotective agent against stroke: its translation from laboratory research to clinical application. *Neuropeptides* 2011; **45**: 359-368 [PMID: 21592568 DOI: 10.1016/j.npep.2011.04.002]
 - 75 **Yanagishita T**, Tomita M, Itoh S, Mukae S, Arata H, Ishioka H, Geshi E, Konno N, Katagiri T. Protective effect of captopril on ischemic myocardium. *Jpn Circ J* 1997; **61**: 161-169 [PMID: 9070972]
 - 76 **Tyrrell DJ**, Bharadwaj MS, Van Horn CG, Kritchewsky SB, Nicklas BJ, Molina AJ. Respirometric Profiling of Mitochondria and Blood Cells Are Associated With Differences in Gait Speed Among Community-Dwelling Older Adults. *J Gerontol A Biol Sci Med Sci* 2015; **70**: 1394-1399 [PMID: 25030980 DOI: 10.1093/gerona/glu096]
 - 77 **Tyrrell DJ**, Bharadwaj MS, Van Horn CG, Marsh AP, Nicklas BJ, Molina AJ. Blood-cell bioenergetics are associated with physical function and inflammation in overweight/obese older adults. *Exp Gerontol* 2015; **70**: 84-91 [PMID: 26226578 DOI: 10.1016/j.exger.2015.07.015]
 - 78 **Zharikov S**, Shiva S. Platelet mitochondrial function: from regulation of thrombosis to biomarker of disease. *Biochem Soc Trans* 2013; **41**: 118-123 [PMID: 23356269 DOI: 10.1042/BST20120327]
 - 79 **Ladd AC**, Keeney PM, Govind MM, Bennett JP. Mitochondrial oxidative phosphorylation transcriptome alterations in human amyotrophic lateral sclerosis spinal cord and blood. *Neuromolecular Med* 2014; **16**: 714-726 [PMID: 25081190 DOI: 10.1007/s12017-014-8321-y]
 - 80 **Ravi S**, Mitchell T, Kramer PA, Chacko B, Darley-Usmar VM. Mitochondria in monocytes and macrophages-implications for translational and basic research. *Int J Biochem Cell Biol* 2014; **53**:

202-207 [PMID: 24863362 DOI: 10.1016/j.biocel.2014.05.019]

- 81 **Chacko BK**, Kramer PA, Ravi S, Benavides GA, Mitchell T, Dranka BP, Ferrick D, Singal AK, Ballinger SW, Bailey SM, Hardy RW, Zhang J, Zhi D, Darley-USmar VM. The bioenergetic health index: A new concept in mitochondrial translational research. *Clin Sci (Lond)*

2014; **127**: 367-373 [PMID: 24895057 DOI: 10.1042/CS20140101]

- 82 **Gorgey AS**, Dolbow DR, Dolbow JD, Khalil RK, Gater DR. The effects of electrical stimulation on body composition and metabolic profile after spinal cord injury--Part II. *J Spinal Cord Med* 2015; **38**: 23-37 [PMID: 25001669 DOI: 10.1179/2045772314Y.0000000244]

P- Reviewer: Berra LV, Rabchevsky AG **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Lu YJ



Magnetic resonance imaging after anterior cruciate ligament reconstruction: A practical guide

Alberto Grassi, James R Bailey, Cecilia Signorelli, Giuseppe Carbone, Andy Tchonang Wakam, Gian Andrea Lucidi, Stefano Zaffagnini

Alberto Grassi, Cecilia Signorelli, Giuseppe Carbone, Andy Tchonang Wakam, Gian Andrea Lucidi, Stefano Zaffagnini, Laboratorio di Biomeccanica ed Innovazione Tecnologica, Istituto Ortopedico Rizzoli, 40136 Bologna, Italy

James R Bailey, Department of Orthopaedic Surgery, Duke Sports Sciences Institute, Duke University Medical Center, Durham, NC 27710, United States

Stefano Zaffagnini, Unita' Operativa di Ortopedia, Dipartimento Rizzoli-Sicilia, 90011 Bagheria, Italy

Author contributions: Grassi A performed the majority of the writing; Signorelli C, Carbone G and Lucidi GA prepared the figures and tables; Tchonang Wakam A assisted in writing the paper; Zaffagnini S coordinated the writing of the paper and performed critical review; Bailey JR performed language correction and critical review of the contents.

Conflict-of-interest statement: There is no conflict of interest associated with the senior author or other coauthors.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Alberto Grassi, MD, Laboratorio di Biomeccanica ed Innovazione Teconologica, Istituto Ortopedico Rizzoli, Via di Barbiano 1/10, 40136 Bologna, Italy. alberto.grassi3@studio.unibo.it
 Telephone: +39-05-16366507

Received: February 26, 2016
 Peer-review started: February 26, 2016
 First decision: May 13, 2016
 Revised: June 22, 2016

Accepted: August 11, 2016
 Article in press: August 15, 2016
 Published online: October 18, 2016

Abstract

Anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic procedures performed worldwide. In this regard, magnetic resonance imaging (MRI) represents a useful pre-operative tool to confirm a disruption of the ACL and to assess for potential associated injuries. However, MRI is also valuable post-operatively, as it is able to identify, in a non-invasive way, a number of aspects and situations that could suggest potential problems to clinicians. Graft signal and integrity, correct tunnel placement, tunnel widening, and problems with fixation devices or the donor site could all compromise the surgical outcomes and potentially predict the failure of the ACL reconstruction. Furthermore, several anatomical features of the knee could be associated to worst outcomes or higher risk of failure. This review provides a practical guide for the clinician to evaluate the post-surgical ACL through MRI, and to analyze all the parameters and features directly or indirectly related to ACL reconstruction, in order to assess for normal or pathologic conditions.

Key words: Anterior cruciate ligament reconstruction; Magnetic resonance imaging; Graft; Tunnel; Failures; Complications; Anatomic

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: There are several original studies and reviews in the literature that discuss magnetic resonance imaging (MRI) evaluation after anterior cruciate ligament (ACL) reconstruction. However, these are mostly focused on a single aspect such as graft signal intensity, tunnel

placement, joint anatomy, or complications. This is a first known review to summarize all the aspects that should be evaluated through MRI after an ACL reconstruction, in order to perform a complete and global assessment of the post-operative status. The iconographic sections with practical and detailed explanation of measurements will serve as a useful reference for the MRI evaluation after ACL reconstruction in daily clinical practice.

Grassi A, Bailey JR, Signorelli C, Carbone G, Tchonang Wakam A, Lucidi GA, Zaffagnini S. Magnetic resonance imaging after anterior cruciate ligament reconstruction: A practical guide. *World J Orthop* 2016; 7(10): 638-649 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/638.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.638>

INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic procedures performed worldwide. It is considered the standard of care for young active patients who wish to return to sport practice after ACL injury^[1]. Despite the lack of clear evidence of its ability to reduce the onset and progression of knee osteoarthritis (OA), ACL reconstruction is expected to prevent further meniscal and cartilage lesions that could occur in the ACL-deficient knee^[2,3]. Usually, ACL reconstruction is performed arthroscopically (occasionally combined with extra-articular plasty/augmentation) using autologous graft such as Gracilis and Semitendinosus tendons (HS), bone-patellar tendon bone (BPTB), and Quadriceps Tendon (QT), or allogenic grafts such as BPTB, Achilles Tendon, and Posterior or Anterior Tibialis tendons. Graft fixation is obtained through a wide range of fixation devices, different in function, shape, size, material, biomechanical proprieties and positioning. The outcomes of ACL reconstruction are generally good; however, graft rupture or clinical failure can occur in 6%-12% of the cases^[4].

In the field of ACL injury and reconstruction, magnetic resonance imaging (MRI) represents a useful pre-operative tool to confirm a disruption of the ACL and to assess for potential associated injuries. However, MRI is also valuable post-operatively to assess graft healing and maturation, to determine its position, and to evaluate potential complications or re-injury^[5-7]. For example, a survey among expert surgeons of the German Arthroscopy Association (AGA) showed that MRI represents one of the decision-making criteria for return to sport activity in only 4% of those interviewed^[8].

The purpose of this review is to provide a practical guide for the clinician to evaluate the post-surgical ACL through MRI, and to analyze all the parameters and features directly or indirectly related to ACL reconstruction, in order to assess normal or pathologic conditions.

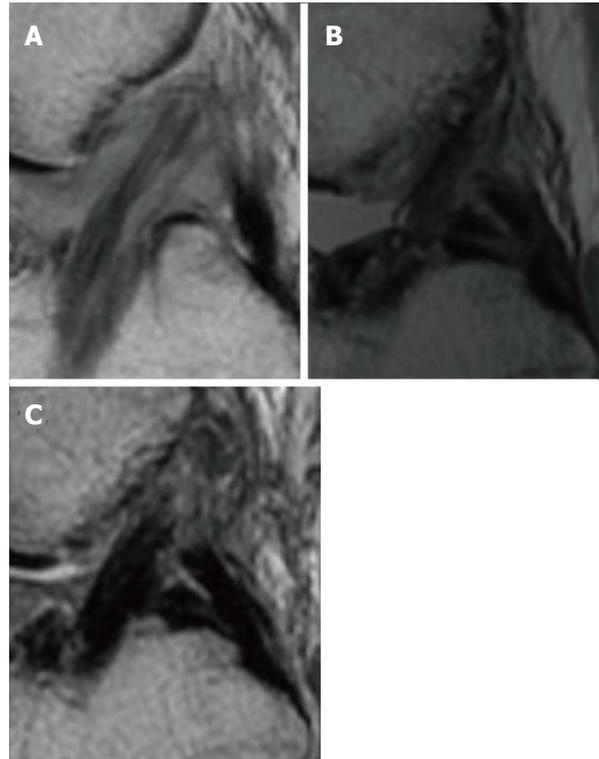


Figure 1 Various graft signal intensity. The signal intensity is usually calculated through the SNQ (signal-digital noise ratio), which is obtained through the following formula: $SNQ = (ACL \text{ graft signal} - PCL \text{ graft signal}) / \text{background signal}$. According to these measurements, we could have a hyperintense graft (A), a graft with reduced intensity signal but not yet analogous to native ACL (B) and a graft iso-intense to PCL (C). PCL: Posterior cruciate ligament; SNQ: Symbol of national quality; ACL: Anterior cruciate ligament.

GRAFT SIGNAL

The signal evaluation of the neo-ligament, whose intensity is generally evaluated with a combined score (Table 1) or with software (Figure 1), represents a dynamic field of research.

General healing process

From the biological point of view, the intra-articular graft undergoes a maturation and remodeling process lasting even beyond 24 mo, and consists of 4 steps: The initial avascular necrosis, the revascularization, cellular proliferation, and final remodeling^[9]. It is generally agreed that initially the graft undergoes necrosis, showing hypocellularity especially in its central part. Cytokines are released as a consequence of necrosis, which then trigger growth factors for cell migration, proliferation, extracellular matrix (ECM) synthesis, and revascularization^[10]. Maximum cellularity is observed during the proliferation phase as the cell number surpasses that of the intact ACL in numerous animal models^[11]. Cell numbers then regress towards the intact ACL cellularity at the end of the proliferation phase. The tissue remodeling phase is started with cell-mediated restructuring of the extracellular matrix as an adaptive response to mechanical loading on the

tendon graft. This whole process from tendon graft toward the acquisition of histologic and biomechanical properties similar to the native ACL is known as "ligamentization".

This process could be indirectly monitored through MRI, as it has been proved that poor biomechanical properties and an incomplete graft maturation are related to a hyperintense graft signal on MRI^[5,7]. Weiler *et al.*^[12] demonstrated in an animal model that a significantly elevated graft signal was present between the 6th and 12th weeks, and this condition was correlated to the lowest tensile stress of the graft (estimated around the 7%-16% of the initial values). However, from the 6th to the 24th month, the signal did not differ from that of the native ACL and the tensile stress increased, reaching around the 60% of the time-zero values. Furthermore, contrast-enhanced MRI with gadolinium showed the return to a graft signal similar to the native ACL by the 24th month, thus suggesting a late remodeling period. From the histological point of view, hyperintense signal was correlated to the presence of new hypervascular and hypercellular reparative tissue.

Despite the normal maturation process, it is important to know that an increase of signal intensity of the new-ACL, especially on the distal two-thirds, may also be due to graft impingement. This complication occurs when the grafts contacts the intercondylar notch during the extension of the knee. This has been implicated in the pathogenesis of the so-called "Cyclops lesion", which consist of a fibrous injury to the anterior side of the graft, close to the site of greatest friction within the notch^[5,13].

BPTB autograft

The structural composition of the graft and the presence or absence of the bone plugs has been shown to present different maturation behaviors and presentations with MRI. When BPTB autograft tendons are used, in the first month the graft usually presents a low-intensity signal in T1 and T2 sequences, similar to the original patellar tendon, mirroring the relatively avascular nature of the donor structure. Subsequently, during the remodeling phase, the graft is wrapped by synovial tissue and vascularized (Figure 2), with the consequent increase of MRI signal up to 16-18 mo. After this period, the graft will shortly reach a signal very similar to original ACL^[5-7].

HS autograft

When Gracilis and Semitendinosus autograft tendons are used, in the 1st month it is possible to not necessarily observe a hypointense signal as with the BPTB graft, because of the multiple layer configuration of the graft that could cause an accumulation of a thin liquid stratum (hyperintense at the MRI) between the individual layers. This finding, sometimes combined with small liquid deposits in the tunnel-graft interface, can remain in the first post-operative year. After that, the maturation process continues similarly to that of the patellar tendon^[5-7]. However, in a recent study on 26 patients undergoing single-bundle ACL reconstruction, it has been

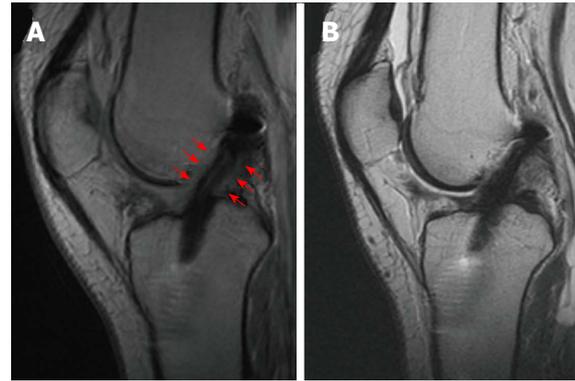


Figure 2 Successful anterior cruciate ligament reconstruction with Gracilis and Semitendinosus autograft with a normal healing process. At the 6th month, it is possible to appreciate in the T2-Fast recovery sat-spin echo (FRFSE) MRI a hyperintense line within the graft body. The graft is surrounded by an intermediate signal intensity tissue (red arrows), representing vascularization and synovialization (A). At the 12th month, the periligamentous signal has disappeared and the graft signal decreased resembling that of PCL (B). PCL: Posterior cruciate ligament; ACL: Anterior cruciate ligament; MRI: Magnetic resonance imaging.

shown that the Gracilis and Semitendinosus autograft demonstrated slower maturation at 6 mo compared to an autograft quadriceps tendon with bone block, when measured with the signal/noise quotient^[14]. The authors proposed the possibility of needing to modify rehabilitation according to the extent of graft maturation to prevent re-injury and maximize patient function.

Allografts

Even allografts exhibit a similar behavior; however, it has been demonstrated that they have a much longer maturing process^[15-17]. This has been confirmed by the persistence of a higher signal intensity compared to autografts for up to 2 years following ACL reconstruction^[18].

In summary, the MRI evaluation of the neo-ligament signal indirectly allows us to obtain valuable information of the state of maturation, giving the clinician precious insight that can help guide rehabilitation and physical activity.

GRAFT INTEGRITY

Apart from incorrect tunnel placement, one of the most common causes of ACL reconstruction failure is a new injury. A new disruption of the reconstructed ligament appears on MRI as increased signal intensity in the T2 sequence within the graft body^[7,19] (Figure 3). However, this should be combined with a concordant clinical examination and a clear medical history of a new trauma. In fact, the mere MRI evaluation could sometimes be misleading, because of the discordance between clinical examination and MRI evaluation. In a series of 50 revision ACL reconstructions with a graft lesion confirmed by arthroscopy and clinical examination, the graft was read intact on MRI evaluation in 24% of cases. The discordance between MRI and clinical evaluation,

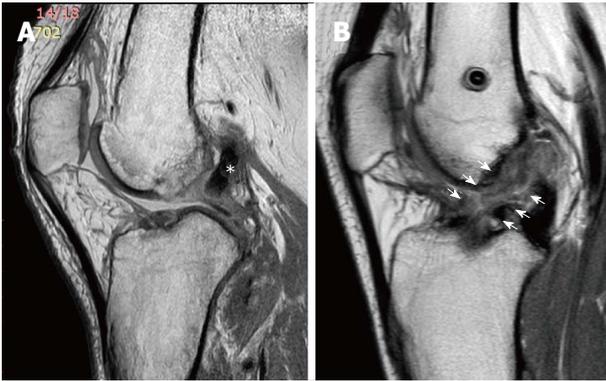


Figure 3 Three years after an anterior cruciate ligament reconstruction with Gracilis and Semitendinosus autograft in a 26-year-old-male. The intercondylar space is occupied by mixoid tissue with slightly hyperintense signal in proton density turbo-spin echo weighted images (white arrows). It is not possible to distinguish the regular course of the graft.

and between MRI and arthroscopic evaluation was 52% and 44% respectively, especially in the cases of an insidious-onset mechanism of injury^[19]. With arthroscopic evaluation as the diagnostic standard, the sensitivity of MRI to diagnose an ACL graft tear was 60%, and specificity 87%.

Therefore, it is possible to see an apparently normal graft on MRI but clinically or arthroscopically injured or elongated. To avoid this discrepancy and to improve the diagnostic power, some authors suggest the use of MR-arthrography, which can increase the sensitivity and specificity toward values near 100%^[5]. Nevertheless the MRI should be considered an additional and not exclusive tool for the assessment of the post-operative ACL.

TUNNEL POSITION

The correct positioning of the femoral and tibia tunnel represents a key technical step for the success of ACL reconstruction surgery. The MRI provides important information about those aspects, especially regarding the graft inclination.

Sagittal plane position

On the sagittal plane of the MRI the front border of the tibial tunnel should be localized behind a line that is tangential to the Blumensaat line (which is the line tangential to the intercondylar roof), without going beyond the midpoint of the proximal tibia with the knee in full extension (Figure 4A). The tibial tunnel center should ideally be located around the 42% mark of the entire sagittal distance of the tibial plateau as measured from the anterior edge of the tibia^[20] (Figure 4A). It has been demonstrated that the native ACL is located between the 28% and 63% mark of the tibial plateau's antero-posterior diameter, with the center at 46%^[21]. If the tunnel is too forward, the risk of impingement of the graft with the intercondylar notch increases, possibly causing extension deficit or a Cyclops lesion (Figure

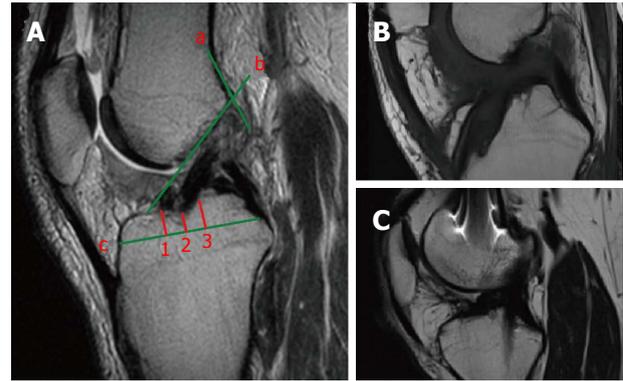


Figure 4 On the sagittal plane, the front border of the tibial tunnel. It should be localized behind a line that is tangential to the Blumensaat line (line b); however, without going beyond the midpoint of the proximal tibia with the knee in full extension. The femoral tunnel should be located at the intersection of the posterior femoral cortex (line a) and the lateral wall of the intercondylar notch (line b). The position of the tibial tunnel entrance is measured as following: the total antero-posterior diameter of the tibial plateau (line c) is measured in the sagittal slice where the tibial entrance is better visualized. The location of the anterior margin of the tunnel is obtained dividing the distance from the anterior tibial plateau margin and the most anterior part of the tunnel entrance (point 1) for the total AP diameter (line c) and multiplying for 100. The location of the posterior margin (point 3) and the center of the tunnel (point 2) are obtained similarly (A). Sagittal view with a tibial tunnel positioned anterior to the midpoint of the tibial plateau diameter, resulting in an increased risk of impingement (B). Sagittal view with a tibial tunnel positioned too posterior, resulting in a vertical graft (C). The native ACL is located between the 31% and 63% of the tibial plateau diameter, with its center at 48%. ACL: Anterior cruciate ligament.

4B), while a tunnel too posterior could lead to a vertical graft (Figure 4) responsible of an incomplete control of knee antero-posterior and rotatory stability^[22]. A controversial matter of debate is the correct positioning of the femoral tunnel. Despite the fact that the most accurate evaluation is obtained through arthroscopy, MRI could be helpful to identify gross malpositioning. It is generally accepted that the femoral tunnel should be located at the intersection of the posterior femoral cortex and the lateral wall of the intercondylar notch^[23] (Figure 4A).

Regarding the bi-dimensional sagittal inclination, considering that the native ACL sagittal inclination ranges between 50°-60°^[24], the graft inclination after ACL reconstruction should not exceed 60° (Figure 5A). A greater laxity could be linked to ACL reconstructions with sagittal graft inclination > 60° (Figure 5B).

Coronal plane position

Similarly, on the coronal plane, the graft inclination should be less than 75° (Figure 6A), as an excessively vertical graft sub-optimally controls rotatory laxity compared with a more horizontally placed graft^[25] (Figure 6B). Usually, the coronal position of the tibial tunnel entrance does not represent an issue in the MRI evaluation after ACL reconstruction, as it is generally in the correct position under the femoral notch in the vast majority of the cases thanks to intra-operative anatomical landmarks; such as the anterior horn of lateral meniscus and the medial tibial eminence.

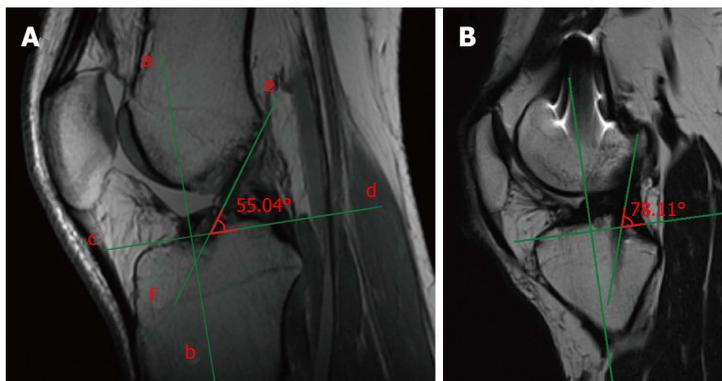


Figure 5 Measurement of the sagittal obliquity of the graft. The inclination is calculated measuring the angle between the perpendicular line (line c and d) to the proximal tibial axis (line a and b), and the line which best defines the course of intra-articular part of the graft (line e and f). A high angle represents a vertical graft in the sagittal plane (A). Vertically positioned graft, with an angle of 78°, far higher than the normal range 50°-60° (B).

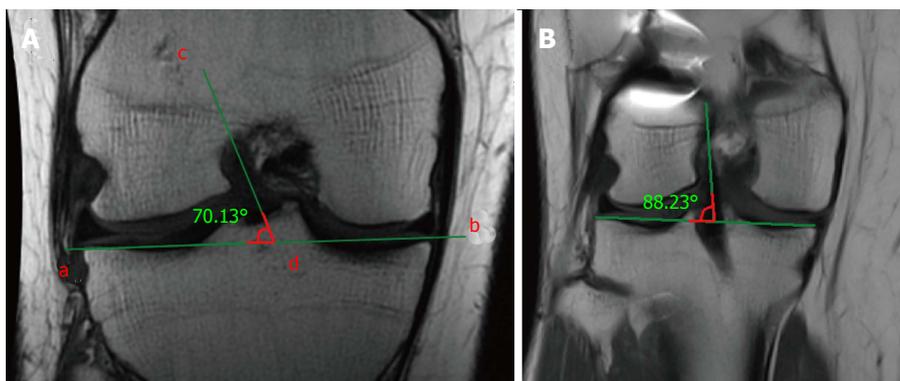


Figure 6 Measurement of the coronal obliquity of the graft. The inclination is calculated measuring the angle between the tangent line to the tibial plateau (a and b) and the line which best defines the course of the intra-articular part of the graft (c and d). A high angle represents a vertical graft in the coronal plane (A). Vertically positioned graft, with an angle of 88°, far higher than the normal value < 75° (B).

Tunnel inclination could therefore be correlated with success or failure of ACL reconstruction. Hosseini *et al*^[26], reported a mean sagittal graft inclination of 69° in patients with failed ACL reconstruction scheduled for a revision procedure. Similarly, Mall *et al*^[24] reported greater laxity in knees with sagittal graft inclination > 60° (Figure 5B); however, this did not affect general outcomes and the ability of these National Football League (NFL) athletes to return to high level sports practice. Furthermore, Fujimoto *et al*^[27] found a mean coronal graft inclination of 79.5° in patients with grade 3 laxity after ACL reconstruction. Several factors could influence graft inclination, such as surgical experience, knee anatomy, and surgical technique. It has been demonstrated that trans-tibial (TT) femoral tunnel drilling tended to result in more vertical grafts in the sagittal plane compared to anteromedial portal (AMP) drilling (72° vs 53°)^[28] or other methods of independent femoral tunnel drilling.

TUNNEL ENLARGEMENT

Tunnel morphology and possible enlargement should be evaluated appropriately using radiographs, computed tomography (CT), or MRI^[29]. It has been demonstrated that intra-observer kappa scores for CT, radiographic and MRI evaluation of tunnel enlargement were 0.66, 0.50 and 0.37 respectively, and inter-observer kappa scores were 0.65, 0.39 and 0.32 respectively. Thus, MRI is considered a sub-optimal and not reliable tool to evaluate the progression of tunnel enlargement, while the CT represents the most reliable one. A precise

tunnel measurement is in fact mandatory, as it could represent an indication for a staged revision procedure (usually with a tunnel diameter > 15 mm). However, through MRI it is possible to identify liquid collection and cyst formation inside the tibial tunnel, responsible of potential tunnel widening (Figure 7). Usually in Gracilis and Semitendinosus ACL reconstruction, such situations could occur within the first post-operative year. A hyperintense signal due to liquid collection in the tendon-tunnel interface could be present; however, with the tendency for spontaneous resolution^[5-7]. Usually, tunnel enlargement occurs within the first 3 month and tends to remain stable up to 2 years if no tunnel malpositioning or graft lack of healing is present.

The exact etiology of tunnel widening is unknown^[30], despite the fact that it has been related to several factors such as mechanical or biological mechanisms. Size mismatch between tunnel and graft dimension could allow sagittal micromotion at the graft-tunnel interface: This phenomenon, known as the “windshield wiper effect”, has been indicated as a potential cause of tunnel enlargement especially in the tibia, proximal to the fixation site. Similarly, longitudinal elongation, known as the “bungee cord effect” could also play a role. The use of a Gracilis and Semitendinosus graft coupled with cortical devices, that produce a low stiffness construct with a long tunnel length, have been demonstrated to be subjected to this phenomenon, leading to tunnel enlargement in the femoral side^[31]. Furthermore, tunnel malposition could generate abnormal stresses and motion of the graft, leading to tunnel lysis. As tunnel enlargement has been noted to stabilize after the first 3 month post-operative,

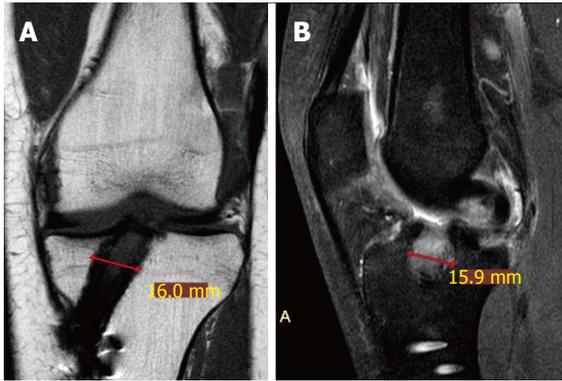


Figure 7 Coronal slice of a proton density spectral attenuated inversion recovery weighted MRI 3.5 years after anterior cruciate ligament reconstruction with gracilis and semitendinosus autograft in a 29-year-old female. It shows tibial tunnel macroscopic enlargement (A). In the sagittal T1 Turbo-Spin Echo weighted image, it is possible to note a cyst with hyperintense signal (B).

it is believed that the bone-to-bone or the tendon-to-bone healing within the tunnel could also influence the mechanical behavior of the graft. For the aforementioned reasons, early and aggressive rehabilitation, could potentially contribute to this phenomenon as well.

Regarding biological factors, it has been proposed that tunnel enlargement has been associated with allograft use secondary to a subclinical immunologic reaction^[32], and to the presence of inflammatory cytokines within synovial fluid between the bone-graft tunnel interfaces, because of their osteolytic activity. Finally, a 12% increase size of the graft due to swelling has been reported through MRI after ACL reconstruction, and the consequent increased pressure within the tunnel could be responsible for necrosis and further cytokine release.

Despite the fact that tunnel enlargement does not appear to adversely affect clinical outcomes in the short term, the long-term relationship with potential knee laxity or increased traumatic failure is unknown^[30]. Moreover, large tunnels could seriously complicate the revision procedure, especially regarding graft placement and fixation, sometimes requiring a staged procedure.

FIXATION DEVICES

Fixation devices can be an issue in ACL post-operative MRI evaluation, because metallic devices could be responsible for disturbing artifacts (Figure 8). However, artifacts derived from metallic devices such as interference screws can be managed with software techniques to reduce metallic-hardware artifacts, reduction of slice thickness, and use of interecho spacing or short tau inversion recovery (STIR) techniques^[33]. The use of bioabsorbable devices reduce the problems related to artifacts. However, despite possible artifacts due to fixation devices, their macroscopic mobilization, migration or rupture could be easily evidenced on MRI, and represent the cause of a potential reconstruction failure. Interference screws can migrate inside the joint damaging articular cartilage; suspensory extra-cortical systems can move inside



Figure 8 Proton density fat saturation coronal magnetic resonance imaging. The metal interference screw on the femoral side (black asterisk) is responsible of marked artifact that could hinder the evaluation of tunnel placement, differently from the bioabsorbable interference screw on the tibial side (white asterisk).

the tunnel causing reduction of graft tensioning; cross pin fixation can migrate inside the soft tissues irritating muscles or tendons; while bioabsorbable materials can generate foreign-body inflammatory reaction. The latter circumstance could represent a severe event, due to an immune-mediate response. The production of inflammatory cytokine and the creation of a granuloma inside the bone around the screw or even in the surrounding soft-tissues, could possibly compromise the trabecular architecture weakening the bone^[34]. Normally, bioabsorbable screws made in Poly-L-lactide (PLLA) or hydroxyapatite-PLLA have been reported to reabsorb slowly, necessitating up to 4 years to degrade^[35]. Poly-D-L-lactide (PDLLA) screws have been reported clearly visible with MRI at 6-8 mo, show fragmentation and connective tissue ingrowth at 12-16 mo, and can be fully reabsorbed after 22 mo^[36]. Differently, Polyglycolic Acid (PGA) screws have been shown to be completely reabsorbed even after 6-12 mo^[37].

DONOR SITE PATHOLOGY

The MRI could be considered a precious tool also to evaluate aspects not directly relating to the neo-ACL, but closely related to reconstruction surgery, as those deriving from graft harvesting.

BPTB autograft

For example, the patellar tendon after the harvesting of its middle third, could appear thickened with enhanced signal in T1 and T2 sequences^[38] (Figure 9). A gap between the medial and lateral third of the patellar tendon could be present, despite the fact it tends to disappear with time (Figure 10). In this regard, MRI studies have revealed the permanence of the tendon gap even after 10 years from reharvesting, and an increase of tendon thickness from 2 to 10 years, significantly higher compared to normal tendon^[39]. Although rare, a patellar fracture, patellar tendon tears, bursitis or hematoma, especially after BPTB graft reharvesting, can be observed.

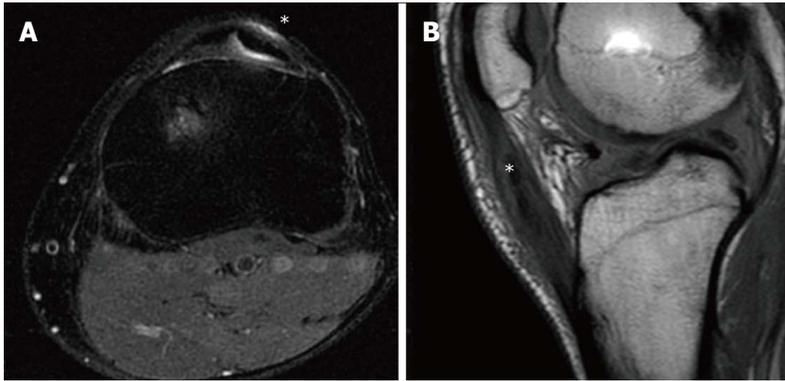


Figure 9 Anterior cruciate ligament reconstruction with bone-patellar tendon bone autograft in a 30-year-old male at 2 years of follow-up. Donor site pathology is displayed as a hyperintense signal (asterisk) in the proton-density fat saturation axial images surrounding the split patellar tendon (A). In the sagittal proton density weighted slice, the post-operative patellar tendinopathy is displayed as an increase of signal intensity within the tendon itself (asterisk), that resulted in an enlarged and swollen tendon (B).

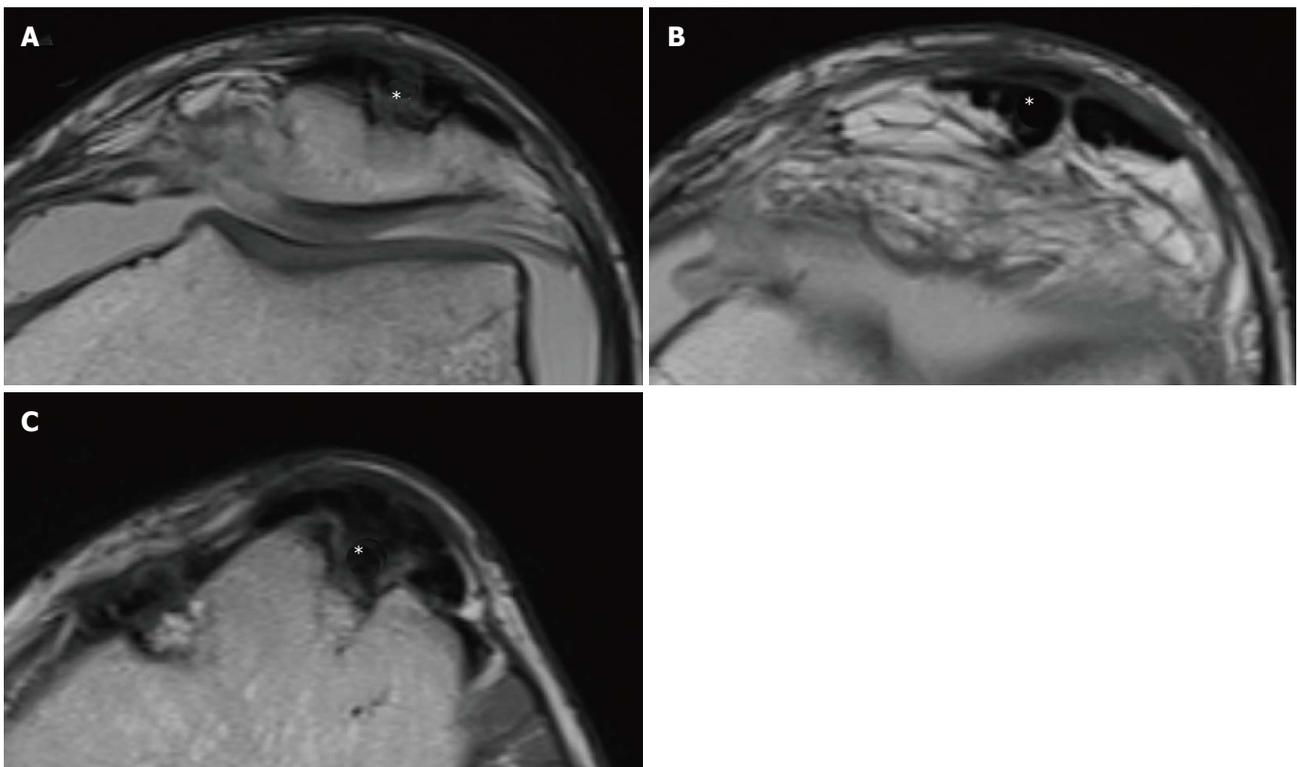


Figure 10 Natural history of bone-patellar tendon bone harvesting in a 21-year-old male. It is possible to appreciate a bone defect (asterisk) on the anterior surface of the patella (A), the split hypointense patellar tendon (asterisk) (B), and another squared bone defect (asterisk) at the level of the central part of the anterior tibial tubercle (C).



Figure 11 Sagittal proton density weighted images of anterior cruciate ligament reconstruction with Gracilis and Semitendinosus Autograft in a 26-year-old male at 1.5 years follow-up. It is possible to appreciate a localized area of low to intermediate signal intensity extending anterior to the distal anterior cruciate ligament graft (black arrows) consistent with local arthrofibrosis.

Sometimes, the Hoffa fat-pad could present an inflammatory reaction, highlighted by a hyperintense T2 signal at MRI fat-suppression sequences, due to hypertrophy and edema.

Another relatively frequent complication that can occur in the anterior knee compartment often related to graft harvesting is arthrofibrosis (Figure 11). Defined as a generic condition of post-operative stiffness (either extension or flexion), arthrofibrosis is believed to occur from ACL reconstruction being performed before post-traumatic inflammation has subsided or secondary to prolonged immobilization after ACL reconstruction. The arthrofibrosis can be diffuse or focal, and presents as an area of low-intermediate signal intensity extending anterior to the distal ACL^[6] (Table 1).

HS autograft

Regarding the “pes-anserinus”, it occasionally is subjected

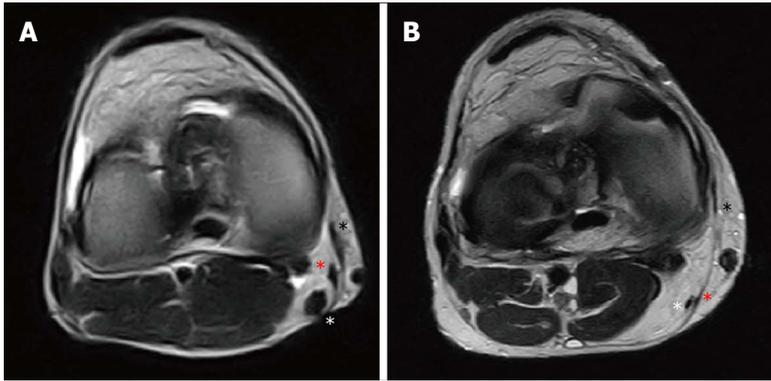


Figure 12 Natural history of Gracilis and Semitendinosus harvesting. Two years after anterior cruciate ligament reconstruction in a 21-year-old male, in the axial view it is possible to appreciate a well represented “pes anserinus” with regenerated Sartorius fascia (black asterisk), Gracilis tendon (red asterisk) and hypertrophic Semitendinosus tendon (white asterisk) (A). Conversely, seven years after anterior cruciate ligament reconstruction in a 35-year-old male, it is possible to identify the Sartorius fascia (black asterisk) with a thin and hypotrophic Gracilis (red asterisk) and Semitendinosus (white asterisk) tendons (B).

Table 1 Figueroa’s score

Item	Points
Integration: Synovial fluid at tunnel-graft interface	
Positive	1
Negative	2
Ligamentization: Graft signal pattern (> 50%)	
Hypointense	3
Isointense	2
Hyperintense	1
Characterization of graft	
Poor	2
Adequate	3-5

The Figueroa score is based on the sum of the points achieved in the 2 items: 2-points represents an insufficiently mature graft, while a score between 3 and 5 points represents a good ligamentization process and graft integration.

to donor-site pathology. A light fluid collection along the donor site can be present in the first post-operative month, until its complete disappearance around 12-18 mo. Tendon regeneration has been documented to occur through the so-called “lizard’s tail effect”, even if the quality for reharvesting could be questioned^[40]. A 2014 systematic review of 18 publications demonstrated a mean regeneration rate for the semitendinosus and gracilis tendons of 70% or higher^[41]. However, more recent literature supports a complete regeneration of the Semitendinosus during the 3rd-6th month in 60% of the cases, while Gracilis regeneration has been reported to be present after its harvesting in 30% of the cases (Figure 12). Complete regeneration of the whole “pes anserinus” was only noted in 10% of the cases, often with an ectopic re-insertion 1-2 cm below the joint line at the level of Sartorius fascia or medial head of Gastrocnemius. In 15% of the cases, complete absence of both tendons was noted. An initial hypertrophy, followed by a progressive volume reduction was described along the first 2 post-operative years, accompanied by muscular atrophy, retraction and fatty infiltration in up to 90% of the cases^[42].

JOINT MORPHOLOGY AND ACL RECONSTRUCTION

Tibial slope

Christensen *et al*^[43] evaluated the MRI of 35 patients with

early ACL failure and 35 with no evidence of ACL graft failure, particularly medial (Figure 13A) and lateral (Figure 13B) tibial plateau sagittal slope. They found a higher lateral tibial plateau slope in patients that experienced graft failure (8.4° vs 6.5°). They estimated an odd ratio for graft failure of 1.6, 2.4 and 3.8 with a slope increase of 2°, 4° and 6° respectively. These findings were more evident in females. A similar conclusion was presented by Webb *et al*^[44] using lateral radiographs. They described an incidence near 60% of graft re-rupture or contralateral ACL injury in patients with tibial slope > 12°. An increased tibial slope, especially the posterior slope of the lateral tibial plateau, is in fact a recognized risk factor for non-contact ACL injury^[45]. However, there are some controversies in the literature, as some studies describing increased medial tibial plateau being the more important risk factor to ACL injury. Others believe the meniscal slope is a more accurate measure rather than the bony tibial plateau slope. Furthermore, different landmarks for measurement, knee or long-leg X-ray, use of MRI, and other features, increase the variability of the measurement and the absence of complete agreement regarding this issue. However, despite the controversy in the literature, it is well accepted that increasing the posterior slope overall increases risk of ACL injury or graft failure.

Notch shape

Notch shape is also considered a risk factor for non-contact ACL injury. A narrow notch has been measured in ACL-deficient patients, probably accounting for a smaller and weaker ACL compared to healthy patients with a wider notch^[46]. Furthermore, in the setting of ACL reconstruction, Fujii *et al*^[13] found a smaller notch cross-sectional area (Figure 14) in patients that developed the “cyclops lesion” due to notch impingement compared to complication-free patients (251.7 mm² vs 335.6 mm²).

Anterior subluxation

Tanaka *et al*^[47] reported an abnormal tibiofemoral relationship at MRI in patients with failed ACL reconstruction. An average of 5.7 mm of anterior tibial subluxation within the lateral compartment was reported, with a value greater than 15 mm in 12.5% of cases (Figure 15). The magnitude of anterior subluxation was 3.9 mm and 3.1 mm greater than the values of normal

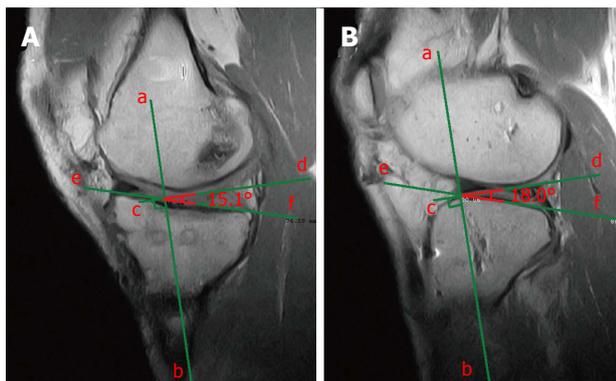


Figure 13 The medial tibial plateau slope is calculated in a sagittal slice passing through the middle-portion of the tibial plateau. As the angle between the perpendicular line (line c and d) to the proximal tibial axis (line a and b) and the line tangent to the tibial plateau (line e and f) (A); the lateral tibial plateau slope is calculated similarly (B). For a correct identification of the proximal tibial axis, it should pass mid-way on two antero-posterior tibial diameters drawn at a distance of 5 cm and 15 cm from the joint line.

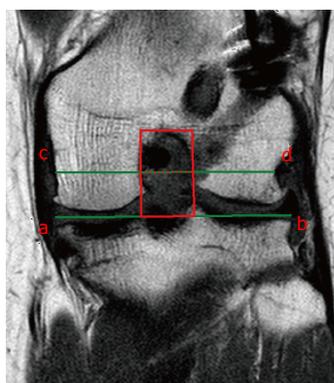


Figure 14 The femoral notch cross sectional area is measured as follows. The coronal slice passing at the middle point of the Blumensaat Line is chosen. The width of the notch (red dotted line) is measured on a line passing through the popliteal groove (line c and d) parallel to the femoral joint surface (line a and b). The height of the notch is the distance between the joint surface and the top of the intercondylar notch. The cross sectional area (red box) is obtained multiplying the width (mm) by the height (mm).

knees and knees with acute ACL tears, respectively. No noteworthy findings were reported for the medial compartment. This association between anterior displacement and failed ACL reconstruction may provide a mechanical explanation of suboptimal clinical results of ACL revision reconstruction.

Tibial plateau and femoral condyles geometry

In the ACL-deficient condition, Musahl *et al.*^[48] noted a narrower lateral tibial plateau in patients with grade II pivot-shift compared to patients with grade I pivot-shift, (35.5 mm vs 30.3 mm) (Figure 16). However, this finding was significant only in female patients. No other anatomical parameters seemed to affect the pre-operative laxity. The authors suggested that bony anatomy contributes to the magnitude of knee laxity in the ACL-deficient knee; therefore, it could be argued that patients with specific anatomical features could represent



Figure 15 The tibial anterior subluxation with respect to the femur is measured as follow. With the magnetic resonance imaging acquired in extension and external rotation, the sagittal slice passing through the insertion of the medial gastrocnemius (medial side) or through the most medial cut of the fibula at the tibiofibular joint (lateral side) is selected. Then, a circle over the subchondral line of the posterior condyle (circle a) and a line tangential to the tibial plateau (line b and c) are drawn. The distance (red asterisk) between a perpendicular line to the tibial plateau passing through its posterior margin (line d and e) and a parallel line tangent to the circle (line f and g) is measured.

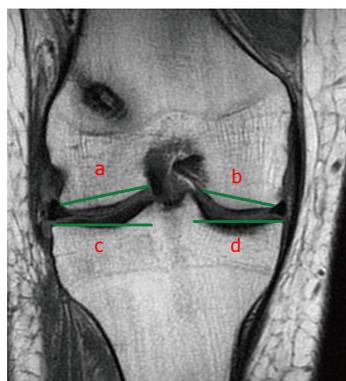


Figure 16 Tibial plateau anatomy is best evaluated by selecting the coronal slice where both tibial spines are visible. Lateral Femoral Condyle (line a) and Medial Femoral Condyle (line b) diameters are measured from borders of corresponding articular cartilage. Lateral Tibial Plateau (line c) and Medial Tibial Plateau (line d) diameters are measured from the intercondylar spine to the border of the corresponding tibial plateau.

patients with a higher risk of sub-optimal results of ACL reconstruction. In these cases of higher pre-operative laxity, the association of a lateral extra-articular plasty could be indicated^[49] (Figure 17).

CONCLUSION

MRI represents an important tool for the post ACL reconstruction evaluation, due to its abilities to identify, in a non-invasive manner, a number of aspects and situations that could suggest potential problems to clinicians. Graft signal and integrity, correct tunnel placement or widening, and problems with fixation devices or donor site could all compromise the surgical outcomes and potentially determine the failure of the ACL reconstruction. However, this tool must not be used in isolation when assessing the post ACL reconstruction status. It should always

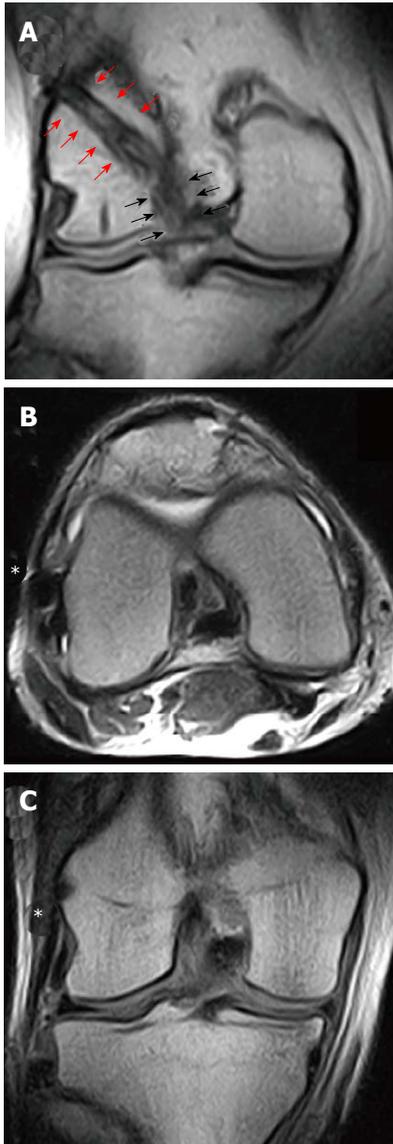


Figure 17 Magnetic resonance imaging evaluation of an anterior cruciate ligament reconstruction with a single-bundle plus lateral extra-articular plasty/augmentation using Gracilis and Semitendinosus Autograft. In the coronal view, it is possible to identify the intra-articular part of the graft (black arrows) that continue proximally above the lateral femoral condyle (red arrows) in the “over-the-top” position (A). The lateral extra-articular plasty (asterisk) could be identified both in axial (B) and coronal view (C) beneath the iliotibial band, extending from the lateral femoral condyle to Gerdy’s tubercle.

be integrated with a careful clinical and medical history evaluation, as only an integrated approach to graft status and functionality is most effective in reducing potential diagnostic mistakes.

REFERENCES

- 1 **Irrazaval S**, Kurosaka M, Cohen M, Fu FH. Anterior cruciate ligament reconstruction. *ISAKOS* 2016; **1**: 38-52 [DOI: 10.1136/jisakos-2015-000011]
- 2 **Fabricant PD**, Lakomkin N, Cruz A, Spitzer E, Lawrence JTR, Marx RG. Early ACL reconstruction in children leads to less meniscal and articular cartilage damage when compared with conservative or delayed treatment. *ISAKOS* 2016; **1**: 10-15 [DOI: 10.1136/

- jisakos-2015-000012]
- 3 **Fabricant PD**, Lakomkin N, Cruz A, Spitzer E, Marx RG. ACL reconstruction in youth athletes results in an improved rate of return to athletic activity when compared with non-operative treatment: a systematic review of the literature. *ISAKOS* 2016; **1**: 2059-7762 [DOI: 10.1136/jisakos-2015-000013]
- 4 **Crawford SN**, Waterman BR, Lubowitz JH. Long-term failure of anterior cruciate ligament reconstruction. *Arthroscopy* 2013; **29**: 1566-1571 [PMID: 23820260 DOI: 10.1016/j.arthro.2013.04.014]
- 5 **Gnannt R**, Chhabra A, Theodoropoulos JS, Hodler J, Andreisek G. MR imaging of the postoperative knee. *J Magn Reson Imaging* 2011; **34**: 1007-1021 [PMID: 22002752 DOI: 10.1002/jmri.22672]
- 6 **Kulezycka P**, Larbi A, Malghem J, Thienpont E, Vande Berg B, Lecouvet F. Imaging ACL reconstructions and their complications. *Diagn Interv Imaging* 2015; **96**: 11-19 [PMID: 24910463 DOI: 10.1016/j.diii.2014.04.007]
- 7 **Naraghi A**, White L. MRI evaluation of the postoperative knee: special considerations and pitfalls. *Clin Sports Med* 2006; **25**: 703-725 [PMID: 16962423 DOI: 10.1016/j.csm.2006.06.007]
- 8 **Petersen W**, Zantop T. Return to play following ACL reconstruction: survey among experienced arthroscopic surgeons (AGA instructors). *Arch Orthop Trauma Surg* 2013; **133**: 969-977 [PMID: 23604790 DOI: 10.1007/s00402-013-1746-1]
- 9 **Janssen RP**, Scheffler SU. Intra-articular remodelling of hamstring tendon grafts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 2102-2108 [PMID: 23982759 DOI: 10.1007/s00167-013-2634-5]
- 10 **Lui PP**, Lee YW, Mok TY, Cheuk YC, Chan KM. Alendronate reduced peri-tunnel bone loss and enhanced tendon graft to bone tunnel healing in anterior cruciate ligament reconstruction. *Eur Cell Mater* 2013; **25**: 78-96 [PMID: 23325540]
- 11 **Unterhauser FN**, Bail HJ, Höher J, Haas NP, Weiler A. Endoligamentous revascularization of an anterior cruciate ligament graft. *Clin Orthop Relat Res* 2003; **(414)**: 276-288 [PMID: 12966303 DOI: 10.1097/01.blo.0000079442.64912.51]
- 12 **Weiler A**, Peters G, Mäurer J, Unterhauser FN, Südkamp NP. Biomechanical properties and vascularity of an anterior cruciate ligament graft can be predicted by contrast-enhanced magnetic resonance imaging. A two-year study in sheep. *Am J Sports Med* 2001; **29**: 751-761 [PMID: 11734489]
- 13 **Fujii M**, Furumatsu T, Miyazawa S, Okada Y, Tanaka T, Ozaki T, Abe N. Intercondylar notch size influences cyclops formation after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1092-1099 [PMID: 24549261 DOI: 10.1007/s00167-014-2891-y]
- 14 **Ma Y**, Murawski CD, Rahnama-Azar AA, Maldjian C, Lynch AD, Fu FH. Graft maturity of the reconstructed anterior cruciate ligament 6 months postoperatively: a magnetic resonance imaging evaluation of quadriceps tendon with bone block and hamstring tendon autografts. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 661-668 [PMID: 25223969 DOI: 10.1007/s00167-014-3302-0]
- 15 **Amendola A**, Stolley MP. What do we really know about allografts? *Clin Sports Med* 2009; **28**: 215-222, vii-viii [PMID: 19306731 DOI: 10.1016/j.csm.2008.10.002]
- 16 **Ekdahl M**, Wang JH, Ronga M, Fu FH. Graft healing in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 935-947 [PMID: 18633596 DOI: 10.1007/s00167-008-0584-0]
- 17 **Gulotta LV**, Rodeo SA. Biology of autograft and allograft healing in anterior cruciate ligament reconstruction. *Clin Sports Med* 2007; **26**: 509-524 [PMID: 17920950 DOI: 10.1016/j.csm.2007.06.007]
- 18 **Li H**, Tao H, Cho S, Chen S, Yao Z, Chen S. Difference in graft maturity of the reconstructed anterior cruciate ligament 2 years postoperatively: a comparison between autografts and allografts in young men using clinical and 3.0-T magnetic resonance imaging evaluation. *Am J Sports Med* 2012; **40**: 1519-1526 [PMID: 22495290 DOI: 10.1177/0363546512443050]
- 19 **Waltz RA**, Solomon DJ, Provencher MT. A Radiographic Assessment

- of Failed Anterior Cruciate Ligament Reconstruction: Can Magnetic Resonance Imaging Predict Graft Integrity? *Am J Sports Med* 2014; **42**: 1652-1660 [PMID: 24821755 DOI: 10.1177/0363546514532335]
- 20 **Howell SM**, Berns GS, Farley TE. Unimpinged and impinged anterior cruciate ligament grafts: MR signal intensity measurements. *Radiology* 1991; **179**: 639-643 [PMID: 2027966 DOI: 10.1148/radiology.179.3.2027966]
- 21 **Frank RM**, Seroyer ST, Lewis PB, Bach BR, Verma NN. MRI analysis of tibial position of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1607-1611 [PMID: 20563557 DOI: 10.1007/s00167-010-1192-3]
- 22 **Lee S**, Kim H, Jang J, Seong SC, Lee MC. Intraoperative correlation analysis between tunnel position and translational and rotational stability in single- and double-bundle anterior cruciate ligament reconstruction. *Arthroscopy* 2012; **28**: 1424-1436 [PMID: 22717211 DOI: 10.1016/j.arthro.2012.03.027]
- 23 **Tomczak RJ**, Hehl G, Mergo PJ, Merkle E, Rieber A, Brambs HJ. Tunnel placement in anterior cruciate ligament reconstruction: MRI analysis as an important factor in the radiological report. *Skeletal Radiol* 1997; **26**: 409-413 [PMID: 9259098 DOI: 10.1007/s002560050256]
- 24 **Mall NA**, Matava MJ, Wright RW, Brophy RH. Relation between anterior cruciate ligament graft obliquity and knee laxity in elite athletes at the National Football League combine. *Arthroscopy* 2012; **28**: 1104-1113 [PMID: 22421564 DOI: 10.1016/j.arthro.2011.12.018]
- 25 **Saupe N**, White LM, Chiavaras MM, Essue J, Weller I, Kunz M, Hurtig M, Marks P. Anterior cruciate ligament reconstruction grafts: MR imaging features at long-term follow-up--correlation with functional and clinical evaluation. *Radiology* 2008; **249**: 581-590 [PMID: 18769016 DOI: 10.1148/radiol.2492071651]
- 26 **Hosseini A**, Lodhia P, Van de Velde SK, Asnis PD, Zarins B, Gill TJ, Li G. Tunnel position and graft orientation in failed anterior cruciate ligament reconstruction: a clinical and imaging analysis. *Int Orthop* 2012; **36**: 845-852 [PMID: 21826407 DOI: 10.1007/s00264-011-1333-4011-1333-4]
- 27 **Fujimoto E**, Sumen Y, Deie M, Yasumoto M, Kobayashi K, Ochi M. Anterior cruciate ligament graft impingement against the posterior cruciate ligament: diagnosis using MRI plus three-dimensional reconstruction software. *Magn Reson Imaging* 2004; **22**: 1125-1129 [PMID: 15527999 DOI: 10.1016/j.mri.2004.08.007]
- 28 **Hantes ME**, Zachos VC, Liantis A, Venouziou A, Karantanis AH, Malizos KN. Differences in graft orientation using the transtibial and anteromedial portal technique in anterior cruciate ligament reconstruction: a magnetic resonance imaging study. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 880-886 [PMID: 19238359 DOI: 10.1007/s00167-009-0738-8]
- 29 **Marchant MH**, Willimon SC, Vinson E, Pietrobon R, Garrett WE, Higgins LD. Comparison of plain radiography, computed tomography, and magnetic resonance imaging in the evaluation of bone tunnel widening after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1059-1064 [PMID: 19953224 DOI: 10.1007/s00167-009-0952-4]
- 30 **Wilson TC**, Kantaras A, Atay A, Johnson DL. Tunnel enlargement after anterior cruciate ligament surgery. *Am J Sports Med* 2004; **32**: 543-549 [PMID: 14977688 DOI: 10.1177/0363546504263151]
- 31 **Clatworthy MG**, Annear P, Bulow JU, Bartlett RJ. Tunnel widening in anterior cruciate ligament reconstruction: a prospective evaluation of hamstring and patella tendon grafts. *Knee Surg Sports Traumatol Arthrosc* 1999; **7**: 138-145 [PMID: 10401649]
- 32 **Fahey M**, Indelicato PA. Bone tunnel enlargement after anterior cruciate ligament replacement. *Am J Sports Med* 1994; **22**: 410-414 [PMID: 8037283 DOI: 10.1177/036354659402200318]
- 33 **White LM**, Buckwalter KA. Technical considerations: CT and MR imaging in the postoperative orthopedic patient. *Semin Musculoskelet Radiol* 2002; **6**: 5-17 [PMID: 11917267 DOI: 10.1055/s-2002-23160]
- 34 **Konan S**, Haddad FS. Femoral fracture following knee ligament reconstruction surgery due to an unpredictable complication of bioabsorbable screw fixation: a case report and review of literature. *J Orthop Traumatol* 2010; **11**: 51-55 [PMID: 20016925 DOI: 10.1007/s10195-009-0079-x]
- 35 **Ma CB**, Francis K, Towers J, Irrgang J, Fu FH, Harner CH. Hamstring anterior cruciate ligament reconstruction: a comparison of bioabsorbable interference screw and endobutton-post fixation. *Arthroscopy* 2004; **20**: 122-128 [PMID: 14760343 DOI: 10.1016/j.arthro.2003.11.007]
- 36 **Achtnich A**, Forkel P, Metzloff S, Zantop T, Petersen W. Degradation of poly-D-L-lactide (PDLA) interference screws (Megafix®). *Arch Orthop Trauma Surg* 2014; **134**: 1147-1153 [PMID: 24899253 DOI: 10.1007/s00402-014-2013-9]
- 37 **Fink C**, Benedetto KP, Hackl W, Hoser C, Freund MC, Rieger M. Bioabsorbable polyglyconate interference screw fixation in anterior cruciate ligament reconstruction: a prospective computed tomography-controlled study. *Arthroscopy* 2000; **16**: 491-498 [PMID: 10882444 DOI: 10.1053/jars.2000.4633]
- 38 **Peterson RK**, Shelton WR, Bomboy AL. Allograft versus autograft patellar tendon anterior cruciate ligament reconstruction: A 5-year follow-up. *Arthroscopy* 2001; **17**: 9-13 [PMID: 11154360 DOI: 10.1053/jars.2001.19965]
- 39 **Lidén M**, Ejerhed L, Sernert N, Bovaller A, Karlsson J, Kartus J. The course of the patellar tendon after reharvesting its central third for ACL revision surgery: a long-term clinical and radiographic study. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 1130-1138 [PMID: 16951974 DOI: 10.1007/s00167-006-0167-x]
- 40 **Yoshiya S**, Matsui N, Matsumoto A, Kuroda R, Lee S, Kurosaka M. Revision anterior cruciate ligament reconstruction using the regenerated semitendinosus tendon: analysis of ultrastructure of the regenerated tendon. *Arthroscopy* 2004; **20**: 532-535 [PMID: 15122146 DOI: 10.1016/j.arthro.2004.01.031]
- 41 **Suijkerbuijk MA**, Reijman M, Lodewijks SJ, Punt J, Meuffels DE. Hamstring Tendon Regeneration After Harvesting: A Systematic Review. *Am J Sports Med* 2015; **43**: 2591-2598 [PMID: 25548149 DOI: 10.1177/0363546514562169]
- 42 **Tsifountoudis I**, Bisbinas I, Kalaitzoglou I, Markopoulos G, Haritandi A, Dimitriadis A, Papastergiou S. The natural history of donor hamstrings unit after anterior cruciate ligament reconstruction: a prospective MRI scan assessment. *Knee Surg Sports Traumatol Arthrosc* 2015; Epub ahead of print [PMID: 26239861 DOI: 10.1007/s00167-015-3732-3]
- 43 **Christensen JJ**, Krych AJ, Engasser WM, Vanhees MK, Collins MS, Dahm DL. Lateral Tibial Posterior Slope Is Increased in Patients With Early Graft Failure After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2015; **43**: 2510-2514 [PMID: 26320223 DOI: 10.1177/0363546515597664]
- 44 **Webb JM**, Salmon LJ, Leclerc E, Pinczewski LA, Roe JP. Posterior tibial slope and further anterior cruciate ligament injuries in the anterior cruciate ligament-reconstructed patient. *Am J Sports Med* 2013; **41**: 2800-2804 [PMID: 24036571 DOI: 10.1177/0363546513503288]
- 45 **Bisson LJ**, Gurske-DePerio J. Axial and sagittal knee geometry as a risk factor for noncontact anterior cruciate ligament tear: a case-control study. *Arthroscopy* 2010; **26**: 901-906 [PMID: 20620789 DOI: 10.1016/j.arthro.2009.12.012]
- 46 **Sonnery-Cottet B**, Archbold P, Cucurulo T, Fayard JM, Bortolotto J, Thauant M, Prost T, Chambat P. The influence of the tibial slope and the size of the intercondylar notch on rupture of the anterior cruciate ligament. *J Bone Joint Surg Br* 2011; **93**: 1475-1478 [PMID: 22058297 DOI: 10.1302/0301-620X.93B11.26905]
- 47 **Tanaka MJ**, Jones KJ, Gargiulo AM, Delos D, Wickiewicz TL, Potter HG, Pearle AD. Passive anterior tibial subluxation in anterior cruciate ligament-deficient knees. *Am J Sports Med* 2013; **41**: 2347-2352 [PMID: 23928320 DOI: 10.1177/0363546513498995]
- 48 **Musahl V**, Ayeni OR, Citak M, Irrgang JJ, Pearle AD, Wickiewicz TL. The influence of bony morphology on the magnitude of the pivot shift. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1232-1238 [PMID: 20376621 DOI: 10.1007/s00167-010-1129-x]
- 49 **Marcacci M**, Zaffagnini S, Marcheggiani Muccioli GM, Neri MP,

Bondi A, Nitri M, Bonanzinga T, Grassi A. Arthroscopic intra- and extra-articular anterior cruciate ligament reconstruction with gracilis

and semitendinosus tendons: a review. *Curr Rev Musculoskelet Med* 2011; 4: 73-77 [PMID: 21594691 DOI: 10.1007/s12178-011-9075-x]

P- Reviewer: Fanter NJ, Seijas R **S- Editor:** Qiu S **L- Editor:** A
E- Editor: Lu YJ



Treatment of the ulnar nerve for overhead throwing athletes undergoing ulnar collateral ligament reconstruction

Matthew S Conti, Christopher L Camp, Neal S Elattrache, David W Altchek, Joshua S Dines

Matthew S Conti, Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY 10021, United States

Christopher L Camp, David W Altchek, Joshua S Dines, Shoulder and Sports Medicine Service, Hospital for Special Surgery, New York, NY 10021, United States

Neal S Elattrache, Kerlan-Jobe Orthopaedic Clinic, Los Angeles, CA 90045, United States

Author contributions: Conti MS, Camp CL and Dines JS wrote the paper; Elattrache NS and Altchek DW reviewed and revised the manuscript.

Conflict-of-interest statement: Authors declare no conflict of interests for this article.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Joshua S Dines, MD, Shoulder and Sports Medicine Service, Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, United States. dinesj@hss.edu
Telephone: +1-516-4821037
Fax: +1-516-4829217

Received: April 23, 2016
Peer-review started: April 24, 2016
First decision: June 6, 2016
Revised: July 15, 2016
Accepted: August 6, 2016
Article in press: August 8, 2016
Published online: October 18, 2016

Abstract

Ulnar nerve (UN) injuries are a common complaint amongst overhead athletes. The UN is strained during periods of extreme valgus stress at the elbow, especially in the late-cocking and early acceleration phases of throwing. Although early ulnar collateral ligament (UCL) reconstruction techniques frequently included routine submuscular UN transposition, this is becoming less common with more modern techniques. We review the recent literature on the sites of UN compression, techniques to evaluate the UN nerve, and treatment of UN pathology in the overhead athlete. We also discuss our preferred techniques for selective decompression and anterior transposition of the UN when indicated. More recent studies support the use of UN transpositions only when there are specific preoperative symptoms. Athletes with isolated ulnar neuropathy are increasingly being treated with subcutaneous anterior transposition of the nerve rather than submuscular transposition. When ulnar neuropathy occurs with UCL insufficiency, adoption of the muscle-splitting approach for UCL reconstructions, as well as using a subcutaneous UN transposition have led to fewer postoperative complications and improved outcomes. Prudent handling of the UN in addition to appropriate surgical technique can lead to a high percentage of athletes who return to competitive sports following surgery for ulnar neuropathy.

Key words: Ulnar nerve; Neuropathy; Ulnar collateral ligament reconstruction; Management; Athletes

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Ulnar nerve (UN) injuries frequently plague overhead athletes due to the strain caused by extreme valgus stress across the elbow during throwing. In this paper, we review common locations of UN compression

and keys to the evaluation. We also discuss the recent literature on treatment of injuries to the UN in overhead athletes and our preferred techniques for addressing UN symptomatology during concomitant UCL reconstruction. Athletes are increasingly being treated with subcutaneous anterior UN transpositions only when appreciable neurologic symptoms are present preoperatively.

Conti MS, Camp CL, Elattrache NS, Altchek DW, Dines JS. Treatment of the ulnar nerve for overhead throwing athletes undergoing ulnar collateral ligament reconstruction. *World J Orthop* 2016; 7(10): 650-656 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/650.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.650>

INTRODUCTION

Ulnar nerve (UN) injuries in the overhead athlete often occur as a result of overuse of the arm during throwing and may exist in isolation or in association with other pathologic processes such as ulnar collateral ligament (UCL) insufficiency^[1-4]. Because of its course along the medial elbow, the UN can be strained in the cubital tunnel (CT) secondary to the extreme valgus stress experienced by the elbow during throwing^[1,2]. Secondary causes of ulnar neuropathy include a traction neuritis as a result of valgus stress, osteophytes, compression caused by adhesions, flexor muscle hypertrophy, or repetitive friction secondary to subluxation of the nerve^[5]. As the second most common entrapment neuropathy of the upper extremity, CT syndrome (CTS) has even been reported in adolescent baseball players in elementary and middle school^[6,7].

Reconstruction of the UCL also places the UN at risk. When Dr. Jobe *et al*^[8] first published his series of UCL reconstructions with concomitant submuscular UN transposition in 16 elite throwing athletes in 1986, he reported postoperative UN complications in five patients, of which, two required a subsequent surgery for neurolysis. However, changes in surgical technique including selective, subcutaneous transposition of the UN have led to improved outcomes in UCL reconstruction and fewer postoperative neurologic complications^[5,9].

UN ANATOMY AND SITES OF COMPRESSION

The UN begins in the anterior compartment of the upper arm before entering the posterior compartment at the arcade of Struthers. At the elbow, the nerve resides in the CT just posterior to the medial epicondyle and exits the CT between the dual heads of the flexor carpi ulnaris muscle (FCU) and into the anterior compartment of the forearm (Figure 1). Nerve compression may occur at numerous sites throughout its course. Additionally, the UN is susceptible to the "double crush" phenomenon,

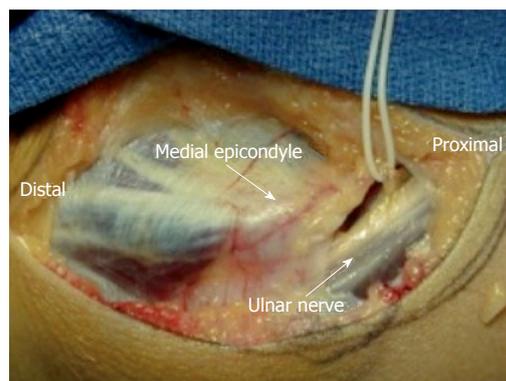


Figure 1 Ulnar nerve anatomy at the elbow. The ulnar nerve courses posterior to the intermuscular septum and adjacent to the triceps. It passes posterior to the medial epicondyle before entering into the cubital tunnel.

which is found when the it is compressed at more than one level^[10]. This occurs because nerves compressed at one site are more easily damaged at another^[11].

The arcade of Struthers, a band that travels from the medial head of the triceps to the medial intermuscular septum in the upper arm, is another common site of compression for the UN. Located approximately 8 cm proximal to the medial epicondyle, the arcade of Struthers present in 70% of the population^[3,9,12,13]. Failure to relieve compression at the arcade of Struthers can lead to persistent UN symptoms despite cubital tunnel release^[3,9,10,12,13]. The UN can also be compressed in patients with a hypertrophy medial triceps, which is commonly observed in throwing athletes^[9]. In a recent series of six adolescent throwers with CTS and a hypertrophic medial triceps, all six patients demonstrated UN compression when the elbow was flexed greater than 90°^[7].

After traversing the arcade of Struthers, the nerve enters the CT as it passes behind the medial epicondyle. The floor of the CT is formed by the olecranon, posteromedial elbow capsule, and UCL, while the roof is created by the CT retinaculum (or arcuate ligament). It has been reported that the space available for the UN within the CT decreases by as much as 55% during elbow flexion^[10]. Additionally, the CT can be narrowed in the presence of a hypertrophic arcuate ligament or anconeus epitrochlearis muscle^[9,14]. Bony abnormalities such as prominent osteophytes near the medial epicondyle or the olecranon can impinge on the nerve in the CT resulting in UN irritation^[9].

Upon exiting the CT, the UN passes between the dual muscle bellies of the FCU. Compression can also occur at the aponeurosis of the FCU. Additionally, repetitive microtrauma can lead to osteophyte formation and hypertrophy of the sublime tubercle at the UCL insertion, which can subsequently compress the nerve at this site^[9].

UN hypermobility leading to subluxation or dislocation anteriorly over the medial epicondyle may also produce symptoms^[6,9]. Subluxation of the UN typically occurs during elbow flexion^[6]. Asymptomatic nerve dislocation

has been reported in 16% of individuals^[15]. Chronic friction as a result of repeated subluxations of the UN in overhead athletes may lead to inflammation and neuropathy^[16].

The valgus stress experienced by the elbow during overhead throwing may also lead to traction neuropathy of the UN. During late-cocking and early acceleration, the valgus force at the elbow has been estimated to be well over 60 N*m with compressive forces exceeding 500 N at the radiocapitellar joint^[17]. This valgus stress, in combination with elbow extension, results in a tensile stress across structures of the medial elbow including the UCL and UN^[5]. Repetitive microtrauma to the UCL can eventually lead to attenuation or failure of the ligament^[5]. The laxity caused by UCL insufficiency may permit increased medial soft tissue stretching that predisposes these athletes to ulnar neuritis^[5]. Aoki *et al.*^[18] found that the maximum strain during the acceleration phase of throwing may lead to nerve injury and compromise its vascular supply. The resultant decreased circulation to the nerve during overhead throwing may be an important factor contributing to ulnar neuropathy.

Additionally, traction on the UN that occurs when the extended elbow is flexed may contribute to nerve injury^[10]. An additional 5.1 mm of UN excursion has been reported as the elbow moves from 10 to 90 degrees^[19]. This longitudinal traction may compromise neural function and increase the likelihood of irritation^[10].

EVALUATING OF THE UN IN THE THROWING ATHLETE

The diagnosis of ulnar neuropathy in the overhead athlete is predominantly based on history and exam. Early symptoms may include diminished sensation, tingling, or a burning type sensation in the small and ring fingers, especially during or after throwing^[5,9]. Elbow flexion may also exacerbate the patient's symptoms^[6]. Athletes may endorse pain along the medial elbow and limitation of elbow extension despite prolonged periods of rest^[7]. Motor symptoms including weakness or atrophy of the intrinsic muscles of the hand are typically late findings seen only in severe or chronic cases^[9]. Symptoms are generally worsened by repetitive valgus stress, and after several innings of throwing, pitchers may complain of heaviness or clumsiness of the hands and fingers^[9]. Patients who suffer from UN subluxation may report a snapping or popping sensation at the medial elbow that occurs with flexion, extension, or throwing^[9].

Physical examination in the throwing athlete must include the entire length of the UN. A thorough assessment of the cervical spine needs to be performed to look for evidence of radiculopathy or degenerative changes^[9]. Neural or vascular compression at the thoracic outlet should also be ruled out. Afterwards, the examiner can shift focus to the medial elbow. Elbow instability as a result of UCL injury or insufficiency is an important underlying cause of ulnar neuritis^[5]. Thus, UCL

evaluation in athletes with suspected UN compression is essential. Valgus laxity should be assessed, and the Moving Valgus Stress Test is one of the more reliable examination maneuvers for UCL insufficiency^[5]. Palpation of the medial elbow may elicit UN tenderness in the cubital tunnel and may be useful to identify coexisting medial epicondylitis or UN subluxation out of the condylar groove, especially as the elbow is flexed and extended^[9,10]. The examiner should ensure that any patient with a subluxating UN does not also have a snapping medial triceps^[20]. This generally presents as a second "snap" that follows the nerve subluxation. Tinel's test involves tapping the nerve from distal to proximal, and a positive test occurs when there is an unpleasant sensation at a site along the course of the nerve, especially if this recreates the patient's symptoms^[10]. In throwing athletes with suspected ulnar neuropathy, special attention should be directed towards the cubital tunnel^[9]. In addition, the elbow flexion test is a provocative maneuver that can be used to reproduce UN symptoms. To perform the elbow flexion test, the elbow is flexed, while the forearm is supinated and the wrist is extended for several minutes^[9]. The elbow flexion test is positive if the UN symptoms are aggravated in this position^[9].

Distally, a full neurovascular examination should be performed. Loss of static two-point discrimination when compared to the contralateral hand, weakness in grip strength, and weakness in pinch strength can all be signs of ulnar neuropathy^[7]. Froment's sign, in which the patient grasps a piece of paper between the thumb and index finger while resisting the examiner's attempt to pull the object from the patient's hand, may be used to test UN function^[10]. Weakness in the hand's intrinsic muscles may be subtle but often presents before changes in forearm extrinsic weakness and grip strength^[9].

Imaging should begin with elbow in multiple planes (anteroposterior, lateral, and oblique views)^[5]. X-rays are evaluated for osteophytes or degenerative changes that may impinge on the UN as well as any previous bony injury, loose bodies, or abnormal calcification^[9]. Magnetic resonance imaging is often utilized to evaluate the soft tissue structures of the elbow such as: The UN, UCL, and possible space occupying lesions or bone spurs^[9]. Electrophysiologic investigations may occasionally be useful to confirm the diagnosis and the location of compression in equivocal cases^[10]. Additionally, electrodiagnostic testing may reveal a secondary compression site ("double crush" phenomenon). Because these studies have a false negative rate reported to be 10% or even higher, they cannot be solely relied on to identify ulnar neuropathy in the throwing athlete^[16].

TREATMENT OF UN COMPRESSION

Conservative management

Initial management of ulnar neuropathy with conservative treatment is appropriate for the overhead throwing

athlete^[5]. Anti-inflammatory medications, cryotherapy, and physical therapy are the mainstays of non-operative treatment^[5]. The athlete should be instructed to avoid throwing or any other activities that cause pain^[5]. The elbow may be splinted, especially at night, for six weeks to immobilize the UN, and the cubital tunnel may be protected using an elbow pad to avoid pressure to the region^[9]. Before returning to sport, deficiencies in throwing mechanics must be identified and corrected^[9]. A gradual interval-throwing program is initiated, and a stretching program for the posterior capsule is often indicated^[9]. Additionally, participation in a strength-training program focusing on dynamic elbow stabilizers is an important part of rehabilitation^[9]. The athlete should be followed clinically for progression of symptoms. For patients who fail to demonstrate improvement following a comprehensive course of conservative management, surgical options may be considered.

Surgical management

Surgical options for ulnar neuropathy at the cubital tunnel include *in situ* decompression, subcutaneous anterior transposition, or in rare cases, submuscular transposition. UN entrapment syndrome was initially treated with submuscular anterior transposition, and Del Pizzo *et al*^[21] demonstrated successful return to play at 3 to 58 mo postoperatively in nine of fifteen (60%) baseball players treated in this fashion. Similarly, the original technique for UCL reconstruction described by Dr. Jobe *et al*^[8] consisted of release of the flexor-pronator mass from its insertion and concomitant UN submuscular transposition. However, of the sixteen elite throwing athletes included in the initial cohort, UN symptoms persisted in five patients post-operatively^[8]. A follow-up series by Conway *et al*^[22] of 71 athletes (including the sixteen athletes from the original study), who underwent UCL reconstruction and concomitant submuscular nerve transposition found postoperative ulnar neuropathy in 15 (21%) patients, and 9 of these patients went on to require further decompression surgery. Subsequent changes in surgical technique led to improved handling of the nerve and alternative strategies that did not require release of the flexor-pronator muscle origin^[9].

Rettig and Ebben^[23] demonstrated excellent outcomes with anterior subcutaneous UN transposition in twenty athletes who had failed non-operative treatment. The athletes were followed for an average of 19 mo postoperatively, and 19 of 20 (95%) patients were asymptomatic at that time^[23]. The patients returned to play at an average of 12.6 wk^[23]. Similarly, Andrews and Timmerman^[24] published their results on an anterior subcutaneous transfer in eight professional athletes in 1995. They reported postoperative ulnar neuropathy in only 11% of cases, and seven of the athletes (88%) returned to their previous level of play for a minimum of one year^[24]. Azar *et al*^[25] reported only one case of postoperative transient ulnar neuropathy in 91 throwing athletes following UCL reconstruction and subcutaneous UN transposition. They

found that 90% (9 of 10) of athletes with preoperative symptoms of ulnar neuritis demonstrated resolution of those symptoms postoperatively^[25]. Another study in high school aged baseball players undergoing subcutaneous UN transposition reported a 7% incidence of transient ulnar neuropathy and 74% of these athletes were able to return to their previous level of sport for at least a year^[26]. Although no studies have directly compared subcutaneous and submuscular transposition of the UN, the reported rates of postoperative complications appear to be lower in the subcutaneous group.

More recently, many authors have recommended against obligatory UN transposition^[1,27-29]. In one study of 83 athletes who underwent UCL reconstruction without nerve transposition, transient neurogenic symptoms were reported in only 4 (5%) patients post-operatively, and all resolved completely with non-operative care^[27]. In this work, 20 (24%) patients had preoperative UN symptoms^[27]. They hypothesized that not exposing or dissecting the UN minimized the risk of nerve injury^[27]. Other authors only consider transposition of if neurologic symptoms are present preoperatively^[28,29]. Koh *et al*^[28] and Paletta *et al*^[29] both reported low rates of postoperative UN complications (5% and 4%, respectively). Between the two studies, only one patient required subsequent UN transposition^[28]. A more recent systematic review of 378 patients undergoing UCL reconstruction did not support obligatory UN transposition^[1]. In this work, those treated with routine nerve transposition demonstrated a lower rate of "excellent" results (75% vs 89%) and were twice as likely to demonstrate signs of postoperative ulnar neuropathy compared with those treated without transposition^[1]. However, some authors feel that *in situ* decompression should not be used in the overhead athlete because it fails to address the increased tension experienced during the throwing motion^[9].

AUTHORS' PREFERRED TECHNIQUES FOR ADDRESSING THE UN DURING UCL RECONSTRUCTION

In patients without UN symptomatology, we do not routinely expose, decompress, or transpose the UN during UCL reconstruction. For the UCL reconstruction, we utilize the docking technique for humeral fixation and a muscle splitting approach to access the ligament^[30]. Because the docking technique utilizes a socket on the humeral side, the *in situ* nerve is at less risk for injury than it would be when drilling full tunnels as described in the Modified Jobe technique. Great care is taken throughout the procedure to ensure that the course of the UN is well understood, and the nerve is protected during every step, especially during drilling. For patients with UN symptoms, we generally decompress and subcutaneously transpose the nerve during UCL reconstruction. Submuscular transposition is generally reserved for rare cases that have failed a prior subcutaneous transposition despite adequate proximal

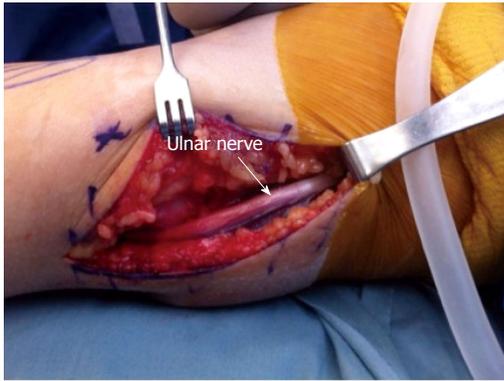


Figure 2 Dissection of the ulnar nerve. The ulnar nerve is identified proximal to the cubital tunnel and posterior to the medial intermuscular septum. Dissection of the nerve begins proximally at the arcade of Struthers and is continued distally to the two heads of the flexor carpi ulnaris muscle.

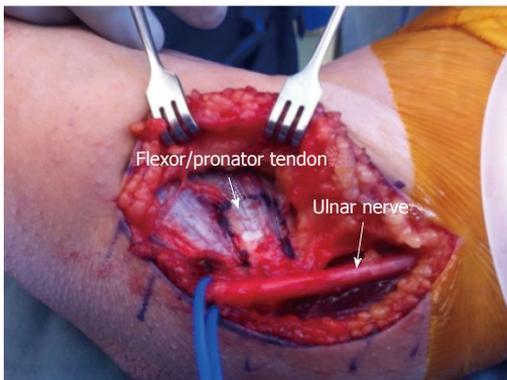


Figure 3 Protection of ulnar nerve. The surgeon must be aware of the anatomy of the ulnar nerve and protect it until the ulnar collateral ligament reconstruction is complete.

and distal decompression.

Subcutaneous transposition is accomplished using the V-sling technique as of Tan *et al.*^[31]. After identifying the UN posterior to the intermuscular septum and proximal to the cubital tunnel, it is carefully dissected free proximally and distally (Figure 2). If transposition is planned, we decompress the nerve at least 10 cm proximally and 10 cm distally from the elbow joint. The nerve is then protected until the UCL reconstruction is complete (Figure 3). Following the UCL procedure, the UN is transposed anterior to the medial epicondyle and thoroughly inspected for any sites of compression such as the medial triceps tendon proximally or the FCU fascia distally. Further decompression is completed as needed. Once it is completely free in the transposed position, a thin slip of the medial intermuscular septum is harvested to serve as a sling to hold it in place. This thin band is excised from the septal fascia beginning 8 cm above the epicondyle. It is dissected distally but is left attached at its distal insertion on the medial epicondyle. The strip is subsequently sutured to the flexor-pronator fascia in an inverted V-shape, which prevents the nerve from migrating behind the epicondyle (Figures 4 and 5).

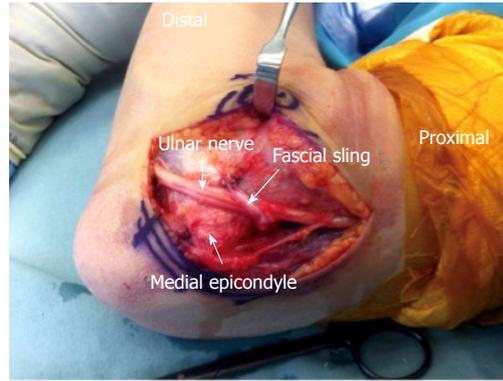


Figure 4 Anterior subcutaneous transposition of the ulnar nerve in flexion. A band of medial intermuscular septum is used as a sling to hold the nerve in place. One end of the band is excised beginning 8 cm proximal to the medial epicondyle, and the other end is left attached to the medial epicondyle. The strip is sutured onto the fascia overlying the flexor-pronator musculature.

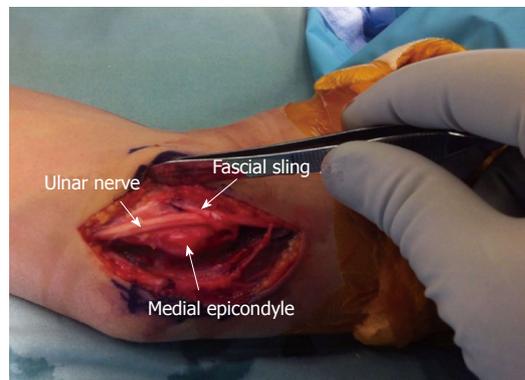


Figure 5 Anterior subcutaneous transposition of the ulnar nerve in extension. The inverted V-shaped sling prevents the nerve from falling behind the medial epicondyle.

The postoperative rehabilitation protocol following transposition of the UN with concomitant UCL reconstruction is determined by the reconstructive procedure rather than the nerve decompression. In these cases of UCL reconstruction, we place the patient in a split post-operatively. The splint is replaced with a hinged elbow brace one week following surgery. While wearing the brace, elbow ROM is initially permitted from 30° to 90°, and this is advanced to 15° to 105° from weeks 3 to 5. At week 6, the brace is discontinued, and formal physical therapy is initiated. From weeks 6 to 12, the focus of PT is on elbow ROM, and shoulder and wrist strength and ROM. This is advanced as tolerated. Beginning at 16th week, a formal throwing program is initiated if the patient has met all milestones up to this point. Throwing begins at a distance of 45 feet on flat ground and is slowly advanced as tolerated. If the patient is able to throw 180 feet on flat ground without pain at the 7- to 9-mo mark, throwing from the mound is permitted. This is slowly advanced over the next 3 mo with the goal of returning the athlete to competitive pitching from a mound between 12 and 18 mo.

CONCLUSION

Recent trends in the treatment of UN injuries in the overhead athlete favor reserving nerve decompression and transposition for instances in which there are appreciable UN symptoms present prior to surgery^[1,27-29]. In cases of isolated ulnar neuropathy in athletes, *in situ* decompression or subcutaneous anterior transposition appear to have more favorable outcomes than submuscular transposition although the techniques have not yet been compared head to head. As the surgical approach for UCL reconstructions has evolved from flexor-pronator detachment to a more tissue friendly muscle-splitting approach, patients with UN symptoms who are undergoing UCL reconstruction are better suited with *in situ* decompression or subcutaneous transposition rather than submuscular transposition. These changes have led to fewer postoperative UN complications and improved outcomes in these high-demand athletes.

Because the UN lies in close proximity to the operative field during the UCL reconstruction, the surgeon must take great care to protect it throughout the duration of the case. Obtaining a diligent history, performing a detailed physical exam, and proper surgical technique are all critical steps needed to successfully treat throwing athletes with UN symptoms. When appropriate steps are followed, the vast majority of athletes can be expected to return to competitive sports.

REFERENCES

- Vitale MA**, Ahmad CS. The outcome of elbow ulnar collateral ligament reconstruction in overhead athletes: a systematic review. *Am J Sports Med* 2008; **36**: 1193-1205 [PMID: 18490476 DOI: 10.1177/0363546508319053]
- King JW**, Brelford HJ, Tullos HS. Analysis of the pitching arm of the professional baseball pitcher. *Clin Orthop Relat Res* 1969; **67**: 116-123 [PMID: 5361189 DOI: 10.1097/0003086-196911000-00018]
- Keefe DT**, Lintner DM. Nerve injuries in the throwing elbow. *Clin Sports Med* 2004; **23**: 723-742, xi [PMID: 15474232 DOI: 10.1016/j.csm.2004.04.012]
- Treihhaft MM**. Neurologic injuries in baseball players. *Semin Neurol* 2000; **20**: 187-193 [PMID: 10946738 DOI: 10.1055/s-2000-9827]
- Cain EL**, Dugas JR, Wolf RS, Andrews JR. Elbow injuries in throwing athletes: a current concepts review. *Am J Sports Med* 2003; **31**: 621-635 [PMID: 12860556 DOI: 10.1177/0363546506295026]
- Spinner RJ**. Nerve Entrapment Syndromes. In: Morrey BF, editor. *Its Disord*. 4th edition. Philadelphia: Saunders Elsevier, 2009: 1090-1118 [DOI: 10.1016/B978-1-4160-2902-1.50085-1]
- Aoki M**, Kanaya K, Aiki H, Wada T, Yamashita T, Ogiwara N. Cubital tunnel syndrome in adolescent baseball players: a report of six cases with 3- to 5-year follow-up. *Arthroscopy* 2005; **21**: 758 [PMID: 15944636 DOI: 10.1016/j.arthro.2005.03.030]
- Jobe FW**, Stark H, Lombardo SJ. Reconstruction of the ulnar collateral ligament in athletes. *J Bone Joint Surg Am* 1986; **68**: 1158-1163 [PMID: 3771597]
- Gee AO**, Angeline ME, Dines JS, Altchek DW. Ulnar nerve issues in throwing athletes. In: Dines JS, Altchek DW, editors. *Ulnar Collat. Ligament Inj. A Guid. to Diagnosis Treat*. New York: Springer, 2015: 179-188 [DOI: 10.1007/978-1-4899-7540-9_21]
- Hayton M**, Talwalkar S. Nerve entrapment around the elbow. In: Stanley D, Trail I, editors. 1st edition. Elsevier, 2012: 455-473 [DOI: 10.1016/B978-0-7020-3099-4.00031-X]
- Upton AR**, McComas AJ. The double crush in nerve entrapment syndromes. *Lancet* 1973; **2**: 359-362 [PMID: 4124532 DOI: 10.1016/S0140-6736(73)93196-6]
- Bencardino JT**, Rosenberg ZS. Entrapment neuropathies of the shoulder and elbow in the athlete. *Clin Sports Med* 2006; **25**: 465-487, vi-vii [PMID: 16798138 DOI: 10.1016/j.csm.2006.03.005]
- Glousman RE**. Ulnar nerve problems in the athlete's elbow. *Clin Sports Med* 1990; **9**: 365-377 [PMID: 2183951]
- Li X**, Dines JS, Gorman M, Limpisvasti O, Gambardella R, Yocum L. Anconeus epitrochlearis as a source of medial elbow pain in baseball pitchers. *Orthopedics* 2012; **35**: e1129-e1132 [PMID: 22784916 DOI: 10.3928/01477447-20120621-39]
- Childress HM**. Recurrent ulnar-nerve dislocation at the elbow. *Clin Orthop Relat Res* 1975; **(108)**: 168-173 [PMID: 1139823 DOI: 10.1097/00003086-197505000-00027]
- Zemel NP**. Ulnar neuropathy with and without elbow instability. *Hand Clin* 2000; **16**: 487-495, x [PMID: 10955221]
- Fleisig GS**, Andrews JR, Dillman CJ, Escamilla RF. Kinetics of baseball pitching with implications about injury mechanisms. *Am J Sports Med* 1995; **23**: 233-239 [PMID: 7778711 DOI: 10.1177/036354659502300218]
- Aoki M**, Takasaki H, Muraki T, Uchiyama E, Murakami G, Yamashita T. Strain on the ulnar nerve at the elbow and wrist during throwing motion. *J Bone Joint Surg Am* 2005; **87**: 2508-2514 [PMID: 16264128 DOI: 10.2106/JBJS.D.02989]
- Wright TW**, Glowczewskie F, Cowin D, Wheeler DL. Ulnar nerve excursion and strain at the elbow and wrist associated with upper extremity motion. *J Hand Surg Am* 2001; **26**: 655-662 [PMID: 11466640 DOI: 10.1053/jhsu.2001.26140]
- Spinner RJ**, Goldner RD. Snapping of the medial head of the triceps and recurrent dislocation of the ulnar nerve. Anatomical and dynamic factors. *J Bone Joint Surg Am* 1998; **80**: 239-247 [PMID: 9486730]
- Del Pizzo W**, Jobe FW, Norwood L. Ulnar nerve entrapment syndrome in baseball players. *Am J Sports Med* 1977; **5**: 182-185 [PMID: 907029 DOI: 10.1177/036354657700500502]
- Conway JE**, Jobe FW, Glousman RE, Pink M. Medial instability of the elbow in throwing athletes. Treatment by repair or reconstruction of the ulnar collateral ligament. *J Bone Joint Surg Am* 1992; **74**: 67-83 [PMID: 1734015]
- Rettig AC**, Ebben JR. Anterior subcutaneous transfer of the ulnar nerve in the athlete. *Am J Sports Med* 1993; **21**: 836-839; discussion 839-840 [PMID: 8291635 DOI: 10.1177/036354659302100613]
- Andrews JR**, Timmerman LA. Outcome of elbow surgery in professional baseball players. *Am J Sports Med* 1995; **23**: 407-413 [PMID: 7573648 DOI: 10.1177/036354659502300406]
- Azar FM**, Andrews JR, Wilk KE, Groh D. Operative treatment of ulnar collateral ligament injuries of the elbow in athletes. *Am J Sports Med* 2000; **28**: 16-23 [PMID: 10653538 DOI: 10.1016/s1048-6666(01)80036-7]
- Petty DH**, Andrews JR, Fleisig GS, Cain EL. Ulnar collateral ligament reconstruction in high school baseball players: clinical results and injury risk factors. *Am J Sports Med* 2004; **32**: 1158-1164 [PMID: 15262637 DOI: 10.1177/0363546503262166]
- Thompson WH**, Jobe FW, Yocum LA, Pink MM. Ulnar collateral ligament reconstruction in athletes: muscle-splitting approach without transposition of the ulnar nerve. *J Shoulder Elbow Surg* 2001; **10**: 152-157 [PMID: 11307079 DOI: 10.1067/mse.2001.112881]
- Koh JL**, Schafer MF, Keuter G, Hsu JE. Ulnar collateral ligament reconstruction in elite throwing athletes. *Arthroscopy* 2006; **22**: 1187-1191 [PMID: 17084295 DOI: 10.1016/j.arthro.2006.07.024]
- Paletta GA**, Wright RW. The modified docking procedure for elbow ulnar collateral ligament reconstruction: 2-year follow-up in elite throwers. *Am J Sports Med* 2006; **34**: 1594-1598 [PMID: 16832125 DOI: 10.1177/0363546506289884]
- Rohrbough JT**, Altchek DW, Hyman J, Williams RJ, Botts JD. Medial collateral ligament reconstruction of the elbow using the docking technique. *Am J Sports Med* 2002; **30**: 541-548 [PMID: 12130409]

31 **Tan V**, Pope J, Daluiski A, Capo JT, Weiland AJ. The V-sling: a modified medial intermuscular septal sling for anterior transposition

of the ulnar nerve. *J Hand Surg Am* 2004; **29**: 325-327 [PMID: 15043909 DOI: 10.1016/j.jhsa.2003.11.011]

P- Reviewer: Anand A, Patra SR **S- Editor:** Gong XM **L- Editor:** A
E- Editor: Lu YJ



Posterior ankle impingement syndrome: A systematic four-stage approach

Youichi Yasui, Charles P Hannon, Eoghan Hurley, John G Kennedy

Youichi Yasui, Department of Orthopaedic Surgery, 2nd Teikyo University School of Medicine, Tokyo 173-8606, Japan

Youichi Yasui, Charles P Hannon, Eoghan Hurley, John G Kennedy, Hospital for Special Surgery, New York, NY 10021, United States

Charles P Hannon, 2nd Department of Orthopaedic Surgery, Rush University Medical Center (C.P.H.), Chicago, IL 60612, United States

Eoghan Hurley, 2nd Royal College of Surgeons in Ireland, Dublin, Ireland

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: Kennedy JG is a consultant for Arterioocyte, Inc.; has received research support from the Ohnell Family Foundation, Mr. and Mrs. Michael J Levitt, and Arterioocyte Inc.; is a board member for the European Society of Sports Traumatology, Knee Surgery, and Arthroscopy, International Society for Cartilage Repair of the Ankle, American Orthopaedic Foot and Ankle Society Awards and Scholarships Committee, International Cartilage Repair Society finance board.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: John G Kennedy, MD, MCh, MMSc, FRCS (Orth), Hospital for Special Surgery, 523 East 72nd Street, Suite 507, New York, NY 10021, United States. kennedyj@hss.edu
Telephone: +1-646-7978880

Fax: +1-646-7978966

Received: May 18, 2016

Peer-review started: May 19, 2016

First decision: July 5, 2016

Revised: July 15, 2016

Accepted: July 29, 2016

Article in press: August 1, 2016

Published online: October 18, 2016

Abstract

Posterior ankle impingement syndrome (PAIS) is a common injury in athletes engaging in repetitive plantarflexion, particularly ballet dancers and soccer players. Despite the increase in popularity of the posterior two-portal hindfoot approach, concerns with the technique remain, including; the technical difficulty, relatively steep learning curve, and difficulty performing simultaneous anterior ankle arthroscopy. The purpose of the current literature review is to provide comprehensive knowledge about PAIS, and to describe a systematic four-stage approach of the posterior two-portal arthroscopy. The etiology, clinical presentation, diagnostic strategies are first introduced followed by options in conservative and surgical management. A detailed systematic approach to posterior hindfoot arthroscopy is then described. This technique allows for systematic review of the anatomic structures and treatment of the bony and/or soft tissue lesions in four regions of interest in the hindfoot (superolateral, superomedial, inferomedial, and inferolateral). The review then discusses biological adjuncts and postoperative rehabilitation and ends with a discussion on the most recent clinical outcomes after posterior hindfoot arthroscopy for PAIS. Although clinical evidence suggests high success rates following posterior hindfoot arthroscopy in the short- and mid-term it may be limited in the pathology that can be addressed due to the technical skills required, but the systematic four-stage approach of the posterior two-portal arthroscopy may

improve upon this problem.

Key words: Posterior ankle impingement syndrome; Arthroscopy; Endoscopy; Review; Os trigonum

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A systematic four-stage approach was developed to standardize technical variety of posterior two-portal hindfoot arthroscopy for the treatment of posterior ankle impingement syndrome (PAIS). After making two-portals using the “nick and spread” technique, hindfoot strictures are divided into 4 regions of interest (superolateral, superomedial, inferomedial, and inferolateral) based on the intermalleolar ligament. In each region, anatomical structures are systematically reviewed and treated in regards to the presence of mechanical impingement and inflammation. Clinical evidence suggests high success rates following arthroscopic approach in short- and mid-term follow-up. This technique can help the surgeons optimize the outcomes following two-portal hindfoot arthroscopy for PAIS.

Yasui Y, Hannon CP, Hurley E, Kennedy JG. Posterior ankle impingement syndrome: A systematic four-stage approach. *World J Orthop* 2016; 7(10): 657-663 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/657.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.657>

INTRODUCTION

Posterior ankle impingement syndrome (PAIS) is a spectrum of clinical disorders characterized by posterior ankle pain during plantar flexion or hyper flexion^[1]. PAIS has become more commonly recognized, particularly in athletes because of heightened awareness^[2-4] and more advanced imaging^[5-7]. Conservative treatment may be indicated in the early stage of PAIS, however; approximately 40% patients eventually require surgical intervention due to intractable hindfoot pain.

The traditional open surgical treatment of PAIS through a lateral or medial approach has had good results, however complication rates are high^[8]. Since its introduction in 2000^[1], the posterior two portal hindfoot approach has been adopted by many surgeons for treatment of PAIS. Recently, a systematic review by Zwiers *et al*^[9] highlighted the advantages of the endoscopic approach over the open approach including lower complication rates, shorter recovery time, less blood loss, less postoperative pain, and comparable functional outcomes. However, concerns with the technique remain; including the technical difficulty, relatively steep learning curve, and difficulty performing simultaneous anterior ankle arthroscopy^[3].

This review discusses the etiology of PAIS, the spectrum of clinical disorders it encompasses, its clinical presentation and management. The review provides

Table 1 Posterior ankle impingement syndrome pathology

Osseus lesions	Soft tissue lesions
Stieda process	Flexor hallucis longus tenosynovitis
Os trigonum	Synovitis
Osteophytes	Impingement of the joint capsule
Osteochondral lesion	Impingement of the anomalous muscles
Loose bodies	
Chondromatosis	
Subtalar coalition	

an up-to date assessment of the clinical evidence for the treatment of PAIS and describes a systematic four-stage approach of the posterior two-portal hindfoot arthroscopy.

ETIOLOGY

PAIS pathology can be due to both osseous and/or soft tissue lesions and anatomic variants (Table 1)^[10]. Osseous lesions include a Stieda process (elongated protuberance)^[10], pathological os trigonum (non-fused ossicle found in up to 25% of the normal adult population)^[11], osteophytes, osteochondral lesion (OCL), loose bodies, chondromatosis, and subtalar coalition. In soft tissue lesions, flexor hallucis longus (FHL) tenosynovitis, synovitis, impingement of the joint capsule, and impingement of the anomalous muscles^[12] are described.

CLINICAL PRESENTATION AND DIAGNOSIS

PAIS is characterized by deep posterior ankle pain caused by plantar flexion of the ankle joint^[13]. Pain is described as consistent, sharp, dull and radiating, however, it is usually hard for patients to indicate the exact location of the pain in the hindfoot. It is most commonly seen in athletes who participate in sports that require repetitive plantar flexion such as ballet dancers, soccer players, and downhill runners^[14]. In these athletes PAIS may present acutely after a forced plantar flexion injury or chronically due to overuse. After an acute injury, patients have a robust inflammatory response leading to pain and swelling that manifests in the hindfoot 3-4 wk after the injury. More commonly, PAIS develops over time in these athletes because repetitive flexion causes increased compression and forces on the anatomic structures between the calcaneus and the posterior part of the distal tibia. In these athletes who present with chronic hindfoot pain, the clinician must have a heightened suspicion for PAIS as these symptoms may mimic posterior capsulitis and rheumatoid arthritis. Clinically, it is less common to see PAIS in the non-athletic population or athletes who perform plantar flexion of ankle joint less frequently. In patients who present with chronic hindfoot pain and do not engage in activities with repetitive flexion, anatomic variants may be implicated in the development of PAIS.

A full history and physical examination is critical in the

diagnosis of PAIS. Physical examination should include a complete neurovascular examination as well strength and range of motion assessment. Hindfoot pain aggravated by plantar flexion of the ankle indicates a positive plantar flexion test. A negative plantar flexion test makes a diagnosis of PAIS significantly less likely, but no studies have reported on the specificity or sensitivity of the plantar flexion test in the diagnosis of PAIS. Patients may also be tender over the posteromedial (PM) aspect of the ankle joint. The clinician must pay special attention to the exact location of tenderness, as pain over the posterior tibial tendon may indicate posterior tibial tendon tenosynovitis or dysfunction and not PAIS. To further clarify the location of the pain, the clinician may passively flex and extend the great toe. If the patient is tender during passive or active ROM, it may indicate pathology involving the FHL tendon. A neurologic examination should be performed to exclude tarsal tunnel syndrome, as the pain may be caused by Valleix's sign^[15].

Standard plain X-rays^[6], computed tomography (CT), and magnetic resonance imaging (MRI) are useful for diagnosis and preoperative planning^[7]. In standard plain X-rays, anteroposterior (AP), mortise, and lateral views of ankle joint are commonly used. The lateral view is the most useful view to observe osseous lesions of hindfoot (*e.g.*, Stieda process, os trigonum, osteophytes, loose bodies, chondromatosis, subtalar coalition). Recently, the posterior impingement (PIM) view has been recommended instead of a conventional lateral view for symptomatic hindfoot pain. The PIM view is a lateral, 25-degree external rotation, oblique view of the ankle, which has shown significant superior diagnostic accuracy compared with the lateral view in the detection of os trigonum^[16].

Compared with radiographs, multi-slice helical CT is more useful to evaluate osseous pathologies. CT provides fine detail regarding the size, location, and number of anatomical bony abnormalities^[17]. Many surgeons prefer CT to examine the osteophyte of the tibia that sometimes co-exists with PAIS^[18] and thus often use it to determine whether the anterior or posterior scope would be performed^[18].

MRI is more useful to evaluate soft tissue lesions of the ankle. Of note, the presence and location of anomalous muscles should be evaluated. These anomalous muscles cause PAIS, but also increase the difficulty of operative treatment^[12]. The peroneus quartus is the most commonly reported anomalous muscle, with between 7% and 22% of the population having them, other anomalous muscles such as flexor digitorum accessorius longus only occur in between 1% and 8% of the population^[12].

After the positive plantar flexion test is elicited, the authors prefer to evaluate the condition of the hindfoot structures using standard plain X-ray and MRI. Then, we perform an ultrasound diagnostic injection using a local anesthetic to confirm the diagnosis (Figure 1).

TREATMENT

Conservative treatment

Conservative treatment includes rest, modification of activity, physiotherapy, anti-inflammatory drugs, and ultrasound-guided injections^[19]. Ultrasound-guided injections may be useful in high-level athletes to allow them to finish the season^[20]. Although no substantial evidence has published the success rate with conservative treatment^[19], a small cohort study reported approximately 60% success rates following conservative treatment in PAIS^[21].

Surgical indications

Surgical management is indicated for patients following failure to address symptoms after 3 mo of conservative treatment. However, if athletic patients want to return to athletic activity promptly, then surgical intervention can be recommended early in the treatment process. Options include open treatment or arthroscopic intervention^[3,22,23]. The advantages of arthroscopic procedures for PAIS are that they are less invasive, have a lower risk of postoperative complications, and shorter recovery time for returning to full activity. However, the technical difficulty and relatively steep learning curve are disadvantages^[3]. Additionally, it is difficult to perform simultaneous treatments for anterior ankle pathologies using a posterior two-portal approach, while subtalar arthroscopy or conventional ankle arthroscopy with posterolateral (PL) portal are more available^[24].

For patients who have isolated PAIS, the authors utilize posterior hindfoot arthroscopy. For patients who require operative intervention for both PAIS and ankle anterior pathologies (*e.g.*, anterior impingement syndrome, anterior OCL, degenerative ankle arthritis), the authors prefer to treat anterior pathologies in the supine position with traditional anterior arthroscopic portals, then, switch to the prone position for posterior hindfoot arthroscopy.

Posterior hindfoot arthroscopy - a systematic four-stage approach^[9]

The senior author (John G Kennedy) uses the original posterior two-portal technique, similar to the 21-point systematic surgical approach in anterior ankle arthroscopic surgery^[25]. The senior author utilizes a systematic four-stage approach for posterior hindfoot arthroscopy beginning with a systematic evaluation of the anatomical structures and subsequent operative treatment for pathological abnormalities.

Equipment

Typical arthroscopy equipment used in anterior ankle arthroscopy is required for posterior hindfoot arthroscopy. A 2.7/4.0 mm arthroscope with 30/70 degree viewing angle, a 3.5/4.5 mm shaver for soft tissue debridement, a 4.0 mm aggressive shaver or burr for bony resection,

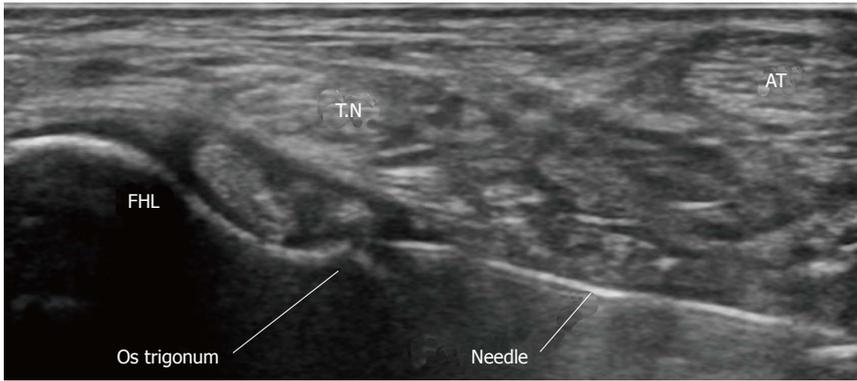


Figure 1 Entosound guided diagnostic injection. AT: Achilles tendon; FHL: Flexor hallucis longus tendon; T.N: Tibial nerve.

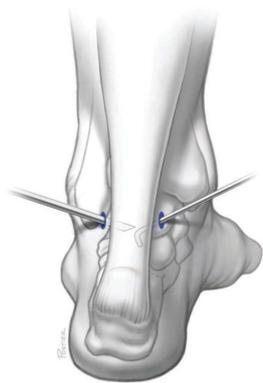


Figure 2 The posterolateral and posteromedial arthroscopic portals.

osteotomy, and fluoroscopy (optional) are used. Sizes of arthroscopes can be selected depending on the surgeon's preference. A thigh tourniquet is necessary to obtain good visualization of hindfoot anatomical structures. Additionally, an irrigation system is useful. The fluid pressure is usually set to 50-60 mmHg, and fluid flow is 0.5 L/min. Although dorsiflexion of hindfoot is usually applied for providing good visualization of the ankle and subtalar joints, a non-invasive distractor is may be applied to assist with visualization.

Patient position

The patient should be positioned in the prone or sloppy lateral position. The senior authors have found that general or spinal anesthetics with a regional block are most effective. The operative foot should be elevated using a support or cushion placed underneath the lower leg, so that the leg is raised approximately 15 cm above the contralateral leg. This position can prevent contact of the arthroscope or instruments with the contralateral side in the operative procedure.

Technique

Marking anatomical landmarks and portal sites:

In posterior hindfoot arthroscopy, a PL and PM portal are most commonly utilized. Prior to incision, landmarks including lateral malleoli (LM), medial malleoli (MM) and Achilles tendon should be marked using a sterile surgical marker. Portal sites should then be marked out.

The portal sites are 1.0 mm anterior to the borders of Achilles tendon and at the level between the horizontal lines running from the inferior poles of MM and tip of LM (Figure 2). The sural nerve can be palpated and its course marked to avoid iatrogenic nerve injury.

Establishing portals:

After all anatomic landmarks and portal sites have been identified and marked, a #11 blade should be used to make 1 cm vertical incisions at the labeled portal sites for the PM and PL portals. Then, subcutaneous blunt dissection using a mosquito clamp is performed *via* both portals. At this time, care must be taken to avoid damage to the sural nerve. The "nick and spread" technique is important to avoid sural neurovascular damages. A 2.7-mm arthroscope sleeve with trocar is carefully advanced *via* a PL portal to touch the posterior aspect of the talus by directing it towards the first interdigital web space. All instruments should be directed towards first interdigital web space to prevent iatrogenic neurovascular bundle injury in the hindfoot. Once the bone can be palpated with the trocar, it is switched out for a 2.7-mm arthroscope.

Creating working space:

Initial visualization is poor because of the fat tissue located behind the posterior aspect of talus. After the shaver blade is confirmed in arthroscopic view, soft tissue is debrided to expose the intermalleolar (IM) ligament using a 3.5 or 4.0 mm aggressive shaver. The shaver blade must always be maneuvered very gently under arthroscopic visualization to avoid iatrogenic injury to healthy tissue.

Systematic four-stage approach to visualization of the hindfoot:

The systematic approach in posterior ankle arthroscopy allows for a full assessment of all structures at the posterior ankle and subtalar joint (Figure 3). The anatomic landmark for defining the quadrants is the IM ligament that has been well described previously^[26,27] based on the IM ligament, the hindfoot structures are divided into 4 regions of interest (superolateral, superomedial, inferomedial, and inferolateral). The authors prefer to start the inspection from the superolateral quadrant and then proceed to the other regions in a counterclockwise fashion for right ankles and a clockwise fashion for left ankles.

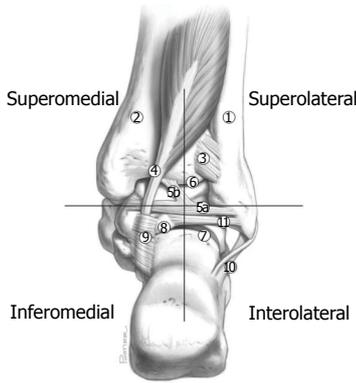


Figure 3 Hindfoot extra-articular structures divided into quadrants as defined by the intermalleolar ligament. (1) Fibula, (2) tibia, (3) posterior-inferior tibiofibular ligament (transverse ligament), (4) flexor hallucis longus tendon, (5a) intermalleolar ligament, (5b) superior tibial insertion of the intermalleolar ligament, (6) tibiotalar joint, (7) subtalar joint, (8) posterolateral talar process, (9) flexor hallucis longus retinaculum, (10) calcaneofibular ligament, and (11) posterior talofibular ligament. Illustration is a copyright of and reproduced with permission from Kennedy JG, MD. Reproduction without express written consent is prohibited.

This quadrant contains the posterior inferior tibiofibular ligament, transverse ligament, and IM ligament. The IM ligament may be associated with PIM^[8,27]. During inspection of the superolateral quadrant, the ankle should be passively plantarflexed to see if any of these ligaments are impinged under direct visualization^[26]. If impingement is present, the related structures should be debrided using a shaver or punch.

The FHL tendon and its associated fibro-osseous tunnel are found in this quadrant. Of note, the neurovascular bundle lies just medial to FHL tendon. It is therefore essential that any instruments should be maneuvered in the area lateral to FHL tendon. Additionally, surgeons should evaluate if the anomalous muscles particularly the peroneus quartus are present^[13]. It is sometime difficult to expose the FHL tendon because of soft tissue cicatrization. In these cases, moving (passive flexion/extension) the great toe may help surgeons identify the FHL tendon.

Tenosynovitis around FHL tendon is a typical finding in patients with hindfoot pain (63% to 85%)^[8,28]. By moving the great toe, impingement of the tendon in its sheath can be identified and resected using a 4.5-mm shaver. A low-lying muscle of FHL can be found, which may cause impingement between the associated bony or soft tissues. Any tenosynovitis or identified impingement should be debrided.

A Stieda process or separate os trigonum can be observed in this region. These bony structures are removed using osteotomes or shaver, with care taken to avoid causing iatrogenic cartilage lesions in the subtalar joint. The scope and shaver are switched in order to gain optimal access to achieve adequate debridement. The posterior talofibular ligament (PTFL) that attaches to these structures may need to be released, however the authors prefer to preserve as much as possible of

the posterior talofibular ligament.

Once those osseous structures are removed, the arthroscope is advanced into the fibro-osseous tunnel, which allows full visualization of the FHL tendon. Any pathology restricting smooth passive movement of the FHL tendon in the fibro-osseous tunnel such as vincula, nodules, or cicatrization should be debrided and removed.

The PTFL and the calcaneofibular ligament (CFL) are found in this region. The PTFL may be thickened and hypertrophied, requiring debridement. In the case of an ankle history of chronic lateral ankle instability, attenuation or scarring of the CFL may be found. Any tenosynovitis or identified impingement should be debrided.

Intra-articular inspection of the talocrural and subtalar joints:

The talocrural joint and subtalar joint are inspected following visualization of all four quadrants of the hindfoot. Both joints can be visualized using same standard portals. Ankle dorsiflexion can allow full visualization of joint surfaces, however, soft tissue distractors are sometimes used to obtain better visualization^[29]. Any pathology detected including OCLs, synovitis, osteophytes, and hypertrophic capsule should be addressed. For OCLs, the authors recommend bone marrow stimulation using a microfracture pic or drilling to produce fibrocartilage repair tissue.

Biologics

Biologics including platelet-rich plasma (PRP) and concentrated bone marrow aspirate (CBMA) may be used at the time of the surgery. These biologic augments are becoming recognized as promising adjuvants that may improve the quality of regenerative tissue and decrease inflammatory responses^[30]. For PAIS, PRP and CBMA are injected into the degenerative tendon or bed of the lesion after irrigation water is stopped. The authors also recommend injecting these biological adjuvants into the joint after the wound is closed to limit the inflammatory response.

Postoperative rehabilitation

A compression bandage is applied after surgery and patients are allowed to be weightbearing as tolerated immediately after surgery. Patients may also begin ranging their ankle as tolerated. The goal of early ROM and weightbearing is to prevent post-operative stiffness and hopefully limit the delay in return to sport^[13,30]. Typically, ankle immobilization is not necessary, unless patients had more significant osseous injury, which may require modifications of the above protocol.

Clinical outcomes following posterior hindfoot arthroscopy

Several clinical studies have reported good short-term clinical results following posterior two-portal hindfoot arthroscopy for PAIS (Table 2)^[28,29,31-41]. A majority

Table 2 Reported clinical outcomes following hindfoot arthroscopy

Ref.	Year	No. of cases (n)	LoE	Follow-up (mo)	Primary outcome measure	Pre-operative score	Post-operative score	Return to sport (wk)
Jerosch <i>et al</i> ^[32]	2006	10	IV	28 (6-61)	AOFAS	43	87	12
Tey <i>et al</i> ^[33]	2007	15	IV	3 (15-63)	AOFAS	84.4	98.5	14.1
Horibe <i>et al</i> ^[34]	2008	11	IV	33.8 (12-58)	AOFAS	71	99	12
Scholten <i>et al</i> ^[28]	2008	55	IV	38 (24-54)	AOFAS	71.1	90	18.9
Willits <i>et al</i> ^[31]	2008	16	IV	3 (6-74)	AOFAS	N/A	91	63
Calder <i>et al</i> ^[35]	2010	27	IV	23 (15-49)	N/A	N/A	N/A	5.9
Noguchi <i>et al</i> ^[36]	2010	12	IV	9.7 (6-14)	AOFAS	68	98.3	5.9
Galla <i>et al</i> ^[37]	2011	30	IV	9.7 (6-14)	AOFAS	60	90	N/A
Ogut <i>et al</i> ^[38]	2011	14	IV	31.6 (8-75)	AOFAS	53.6	84.2	30.6
Nikisch <i>et al</i> ^[39]	2012	80	IV	15.4 (5-59)	N/A	N/A	N/A	N/A
van Dijk <i>et al</i> ^[29]	2009	55	IV	90 (24-480)	AOFAS	75	90	N/A
Lopez-Valerio <i>et al</i> ^[40]	2015	20	IV	78.6 (24-120)	VAS	7.5	0.8	6.7
Dinato <i>et al</i> ^[41]	2015	17	III	N/A	AOFAS	62.9	92.3	15.6
		15				67.9	94	16.3

AOFAS: American Orthopedic Foot and Ankle Society (AOFAS) Score; VAS: Visual Analogue Scale; N/A: Not applicable.

of studies have reported post-operative American Orthopaedic Foot and Ankle Society (AOFAS) Scores greater than 85^[28,29,31-34,36,37,39,41] at short-term follow-up. A recent systematic review by Zwiers *et al*^[9] demonstrated that the mean time to return to full activity was on average 11.3 wk (5.9-12.9 wk) following arthroscopic treatment. Complication rates after posterior hindfoot arthroscopy were also low with 1.8% of patients suffering a major complication and 5.4% of patients suffering a minor complication^[9]. However, the current literature is limited by long-term follow-up studies evaluating the outcomes after posterior hindfoot arthroscopy for PAIS.

CONCLUSION

PAIS is a clinical spectrum of both soft tissue and osseous pathology that is common in athletes who repetitively plantar flex their ankle. Patients who do not respond to conservative management may require operative intervention. While open treatments have showed good success in the short-term for PAIS, posterior hindfoot arthroscopy may lead to equivalent outcomes with less morbidity. Performing two-portal hindfoot arthroscopy in the described systematic four-stage approach allows for standardized evaluation of the anatomic structures of the hindfoot and ultimately to address any pathology that may be present. Clinical outcomes after posterior hindfoot arthroscopy for PAIS are very good in the short-term with low complication rates, however future long-term studies are warranted.

REFERENCES

- 1 van Dijk CN, Scholten PE, Krips R. A 2-portal endoscopic approach for diagnosis and treatment of posterior ankle pathology. *Arthroscopy* 2000; **16**: 871-876 [PMID: 11078550 DOI: 10.1053/jars.2000.19430]
- 2 van Dijk CN, van Bergen CJ. Advancements in ankle arthroscopy. *J Am Acad Orthop Surg* 2008; **16**: 635-646 [PMID: 18978286]
- 3 Coetzee JC, Seybold JD, Moser BR, Stone RM. Management of Posterior Impingement in the Ankle in Athletes and Dancers. *Foot*

- 4 *Ankle Int* 2015; **36**: 988-994 [PMID: 26163559 DOI: 10.1177/1071100715595504]
- 5 Nault ML, Kocher MS, Micheli LJ. Os trigonum syndrome. *J Am Acad Orthop Surg* 2014; **22**: 545-553 [PMID: 25157036]
- 6 Sofka CM. Posterior ankle impingement: clarification and confirmation of the pathoanatomy. *HSS J* 2010; **6**: 99-101 [PMID: 20012503 DOI: 10.1007/s11420-009-9147-2]
- 7 Wiegerinck JI, Vroemen JC, van Dongen TH, Sierevelt IN, Maas M, van Dijk CN. The posterior impingement view: an alternative conventional projection to detect bony posterior ankle impingement. *Arthroscopy* 2014; **30**: 1311-1316 [PMID: 25023737 DOI: 10.1016/j.arthro.2014.05.006]
- 8 Hayashi D, Roemer FW, D'Hooghe P, Guermazi A. Posterior ankle impingement in athletes: Pathogenesis, imaging features and differential diagnoses. *Eur J Radiol* 2015; **84**: 2231-2241 [PMID: 26239710 DOI: 10.1016/j.ejrad.2015.07.017]
- 9 Hamilton WG, Geppert MJ, Thompson FM. Pain in the posterior aspect of the ankle in dancers. Differential diagnosis and operative treatment. *J Bone Joint Surg Am* 1996; **78**: 1491-1500 [PMID: 8876576]
- 10 Zwiers R, Wiegerinck JI, Murawski CD, Smyth NA, Kennedy JG, van Dijk CN. Surgical treatment for posterior ankle impingement. *Arthroscopy* 2013; **29**: 1263-1270 [PMID: 23541613 DOI: 10.1016/j.arthro.2013.01.029]
- 11 Maquirriain J. Posterior ankle impingement syndrome. *J Am Acad Orthop Surg* 2005; **13**: 365-371 [PMID: 16224109 DOI: 10.5435/00124635-200510000-00001]
- 12 Lawson JP. Symptomatic radiographic variants in extremities. *Radiology* 1985; **157**: 625-631 [PMID: 4059550 DOI: 10.1148/radiology.157.3.4059550]
- 13 Best A, Giza E, Linklater J, Sullivan M. Posterior impingement of the ankle caused by anomalous muscles. A report of four cases. *J Bone Joint Surg Am* 2005; **87**: 2075-2079 [PMID: 16140823 DOI: 10.2106/JBJS.D.01916]
- 14 Smyth NA, Murawski CD, Levine DS, Kennedy JG. Hindfoot arthroscopic surgery for posterior ankle impingement: a systematic surgical approach and case series. *Am J Sports Med* 2013; **41**: 1869-1876 [PMID: 23720445 DOI: 10.1177/0363546513489489]
- 15 Smyth NA, Zwiers R, Wiegerinck JI, Hannon CP, Murawski CD, van Dijk CN, Kennedy JG. Posterior hindfoot arthroscopy: a review. *Am J Sports Med* 2014; **42**: 225-234 [PMID: 23868522 DOI: 10.1177/0363546513491213]
- 16 Umans H. Ankle impingement syndromes. *Semin Musculoskelet Radiol* 2002; **6**: 133-139 [PMID: 12077702 DOI: 10.1055/s-2002-32359]
- 17 Wiegerinck JI, Kerkhoffs GMM, Struijs PAA, van Dijk CN. The

- posterior impingement-view: An alternative conventional projection to detect bony posterior ankle impingement. *Arthroscopy* 2014; **30**: 1311-1316 [PMID: 25023737 DOI: 10.1016/j.arthro.2014.05.006]
- 17 **Burghardt AJ**, Link TM, Majumdar S. High-resolution computed tomography for clinical imaging of bone microarchitecture. *Clin Orthop Relat Res* 2011; **469**: 2179-2193 [PMID: 21344275 DOI: 10.1007/s11999-010-1766-x]
 - 18 **Niek van Dijk C**. Anterior and posterior ankle impingement. *Foot Ankle Clin* 2006; **11**: 663-683 [PMID: 16971256 DOI: 10.1016/j.fcl.2006.06.003]
 - 19 **Ribbans WJ**, Ribbans HA, Cruickshank JA, Wood EV. The management of posterior ankle impingement syndrome in sport: a review. *Foot Ankle Surg* 2015; **21**: 1-10 [PMID: 25682399 DOI: 10.1016/j.fas.2014.08.006]
 - 20 **Roche AJ**, Calder JD, Lloyd Williams R. Posterior ankle impingement in dancers and athletes. *Foot Ankle Clin* 2013; **18**: 301-318 [PMID: 23707179 DOI: 10.1016/j.fcl.2013.02.008]
 - 21 **Hedrick MR**, McBryde AM. Posterior ankle impingement. *Foot Ankle Int* 1994; **15**: 2-8 [PMID: 7981792 DOI: 10.1177/107110079401500102]
 - 22 **Marumoto JM**, Ferkel RD. Arthroscopic excision of the os trigonum: a new technique with preliminary clinical results. *Foot Ankle Int* 1997; **18**: 777-784 [PMID: 9429879 DOI: 10.1177/107110079701801205]
 - 23 **Allegra F**, Maffulli N, Cerza F, Delianni E. Postero-medial approach procedure in the supine position for one-step anterior and posterior ankle arthroscopy. *Sports Med Arthrosc* 2009; **17**: 185-189 [PMID: 19680115 DOI: 10.1097/JSA.0b013e3181b12745]
 - 24 **Ferkel RD**. In which position do we perform arthroscopy of the hindfoot--supine or prone? Commentary on an article by Florian Nickisch, MD, et al.: "Postoperative complications of posterior ankle and hindfoot arthroscopy". *J Bone Joint Surg Am* 2012; **94**: e33 [PMID: 22398746 DOI: 10.2106/JBJS.K.01634]
 - 25 **Ferkel RD**, Fischer SP. Progress in ankle arthroscopy. *Clin Orthop Relat Res* 1989; **240**: 210-220 [PMID: 2917435 DOI: 10.1097/00003086-198903000-00027]
 - 26 **Golanó P**, Vega J, de Leeuw PA, Malagelada F, Manzanares MC, Götzens V, van Dijk CN. Anatomy of the ankle ligaments: a pictorial essay. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 557-569 [PMID: 20309522 DOI: 10.1007/s00167-010-1100-x]
 - 27 **Oh CS**, Won HS, Hur MS, Chung IH, Kim S, Suh JS, Sung KS. Anatomic variations and MRI of the intermalleolar ligament. *AJR Am J Roentgenol* 2006; **186**: 943-947 [PMID: 16554561 DOI: 10.2214/AJR.04.1784]
 - 28 **Scholten PE**, Sierevelt IN, van Dijk CN. Hindfoot endoscopy for posterior ankle impingement. *J Bone Joint Surg Am* 2008; **90**: 2665-2672 [PMID: 19047712 DOI: 10.2106/JBJS.F.00188]
 - 29 **van Dijk CN**, de Leeuw PA, Scholten PE. Hindfoot endoscopy for posterior ankle impingement. Surgical technique. *J Bone Joint Surg Am* 2009; **91** Suppl 2: 287-298 [PMID: 19805591 DOI: 10.2106/JBJS.1.00445]
 - 30 **Cassano JM**, Kennedy JG, Ross KA, Fraser EJ, Goodale MB, Fortier LA. Bone marrow concentrate and platelet-rich plasma differ in cell distribution and interleukin 1 receptor antagonist protein concentration. *Knee Surg Sports Traumatol Arthrosc* 2016 Feb 1; Epub ahead of print [PMID: 26831858 DOI: 10.1007/s00167-016-3981-9]
 - 31 **Willits K**, Sonneveld H, Amendola A, Giffin JR, Griffin S, Fowler PJ. Outcome of posterior ankle arthroscopy for hindfoot impingement. *Arthroscopy* 2008; **24**: 196-202 [PMID: 18237704 DOI: 10.1016/j.arthro.2007.08.025]
 - 32 **Jerosch J**, Fadel M. Endoscopic resection of a symptomatic os trigonum. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 1188-1193 [PMID: 16763849 DOI: 10.1007/s00167-006-0089-7]
 - 33 **Tey M**, Monllau JC, Centenera JM, Pelfort X. Benefits of arthroscopic tuberculoplasty in posterior ankle impingement syndrome. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 1235-1239 [PMID: 17589829 DOI: 10.1007/s00167-007-0349-1]
 - 34 **Horibe S**, Kita K, Natsu-ume T, Hamada M, Mae T, Shino K. A novel technique of arthroscopic excision of a symptomatic os trigonum. *Arthroscopy* 2008; **24**: 121.e1-121.e4 [PMID: 18182212 DOI: 10.1016/j.arthro.2007.04.019]
 - 35 **Calder JD**, Sexton SA, Pearce CJ. Return to training and playing after posterior ankle arthroscopy for posterior impingement in elite professional soccer. *Am J Sports Med* 2010; **38**: 120-124 [PMID: 19966105 DOI: 10.1177/0363546509346390]
 - 36 **Noguchi H**, Ishii Y, Takeda M, Hasegawa A, Monden S, Takagishi K. Arthroscopic excision of posterior ankle bony impingement for early return to the field: short-term results. *Foot Ankle Int* 2010; **31**: 398-403 [PMID: 20460066 DOI: 10.3113/FAI.2010.0398]
 - 37 **Galla M**, Lobenhoffer P. Technique and results of arthroscopic treatment of posterior ankle impingement. *Foot Ankle Surg* 2011; **17**: 79-84 [PMID: 21549977 DOI: 10.1016/j.fas.2010.01.004]
 - 38 **Ogut T**, Ayhan E, Irgit K, Sarikaya AI. Endoscopic treatment of posterior ankle pain. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 1355-1361 [PMID: 21311860 DOI: 10.1007/s00167-011-1428-x]
 - 39 **Nickisch F**, Barg A, Saltzman CL, Beals TC, Bonasia DE, Phisitkul P, Femino JE, Amendola A. Postoperative complications of posterior ankle and hindfoot arthroscopy. *J Bone Joint Surg Am* 2012; **94**: 439-446 [PMID: 22398738 DOI: 10.2106/JBJS.K.00069]
 - 40 **López Valerio V**, Seijas R, Alvarez P, Ares O, Steinbacher G, Sallent A, Cugat R. Endoscopic repair of posterior ankle impingement syndrome due to os trigonum in soccer players. *Foot Ankle Int* 2015; **36**: 70-74 [PMID: 25249322 DOI: 10.1177/1071100714552078]
 - 41 **Dinato MC**, Luques IU, Freitas Mde F, Pereira Filho MV, Ninomiya AF, Pagnano RG, Etchebehere M. Endoscopic treatment of the posterior ankle impingement syndrome on amateur and professional athletes. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 1396-1401 [PMID: 26264381 DOI: 10.1007/s00167-015-3747-9]

P- Reviewer: Anand A, Fernandez-Fairen M **S- Editor:** Ji FF

L- Editor: A **E- Editor:** Lu YJ



Retrospective Cohort Study

Effect of body mass index on functional outcome in primary total knee arthroplasty - a single institution analysis of 2180 primary total knee replacements

Shane C O'Neill, Joseph S Butler, Adam Daly, Darren F Lui, Patrick Kenny

Shane C O'Neill, Joseph S Butler, Adam Daly, Darren F Lui, Patrick Kenny, Department of Orthopaedics, Cappagh National Orthopaedic Hospital, Dublin 11, Ireland

Article in press: August 15, 2016
 Published online: October 18, 2016

Author contributions: All the authors contributed to the paper.

Institutional review board statement: The study was reviewed and approved for publication by our Institutional Reviewer.

Informed consent statement: All study participants provided informed written consent about personal and medical data collection prior to enrolment.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at shaneconeill@rcsi.ie.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Shane C O'Neill, MRCS, MCh, Department of Orthopaedics, Cappagh National Orthopaedic Hospital, Finglas, Dublin 11, Ireland. shaneconeill@rcsi.ie
 Telephone: +353-1-8140400

Received: February 15, 2016
 Peer-review started: February 16, 2016
 First decision: March 24, 2016
 Revised: June 20, 2016
 Accepted: August 11, 2016

Abstract

AIM

To evaluate the effect of body mass index (BMI) on short-term functional outcome and complications in primary total knee arthroplasty.

METHODS

All patients undergoing primary total knee arthroplasty at a single institution between 2007 and 2013 were identified from a prospective arthroplasty database. 2180 patients were included in the study. Age, gender, BMI, pre- and post-operative functional scores [Western Ontario and McMaster University Arthritis Index (WOMAC) and SF-36], complications and revision rate were recorded. Patients were grouped according to the WHO BMI classification. The functional outcome of the normal weight cohort (BMI < 25) was compared to the overweight and obese (BMI ≥ 25) cohort. A separate sub-group analysis was performed comparing all five WHO BMI groups; Normal weight, overweight, class 1 obese, class 2 obese and class 3 obese.

RESULTS

With a mean age of 67.89 (28-92), 2180 primary total knee replacements were included. 64.36% (1403) were female. The mean BMI was 31.86 (18-52). Ninety-three percent of patients were either overweight or obese. Mean follow-up 19.33 mo (6-60 mo). There was no significant difference in pre or post-operative WOMAC score in the normal weight (BMI < 25) cohort compared to patients with a BMI ≥ 25 ($P > 0.05$). Sub-group analysis revealed significantly worse WOMAC scores in class 2 obese 30.80 compared to overweight 25.80 ($P < 0.01$) and class 1

obese 25.50 ($P < 0.01$). Similarly, there were significantly worse SF-36 scores in class 2 obese 58.16 compared to overweight 63.93 ($P < 0.01$) and class 1 obese 63.65 ($P < 0.01$). There were 32 (1.47%) superficial infections, 9 (0.41%) deep infections and 19 (0.87%) revisions overall with no complications or revisions in the normal weight cohort (BMI < 25).

CONCLUSION

Post-operative functional outcome was not influenced by BMI comparing normal weight individuals with BMI > 25. Patients should not be denied total knee arthroplasty based solely on weight alone.

Key words: Total knee replacement; Body mass index; Total knee arthroplasty

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We assessed the effect of body mass index (BMI) on short-term functional outcome of 2180 patients that underwent primary total knee arthroplasty at a single institution. Functional outcome was assessed using the Western Ontario and McMaster University Arthritis Index and SF-36 outcome tools. Patients were stratified according to BMI using the WHO classification and results compared. We found no statistical difference in our primary outcome measure, functional outcome of normal weight individuals compared to those with a BMI greater than 25.

O'Neill SC, Butler JS, Daly A, Lui DF, Kenny P. Effect of body mass index on functional outcome in primary total knee arthroplasty - a single institution analysis of 2180 primary total knee replacements. *World J Orthop* 2016; 7(10): 664-669 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/664.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.664>

INTRODUCTION

Total knee arthroplasty (TKA) is an effective surgical treatment of osteoarthritis of the knee, with 700000 procedures performed in the United States annually with the demand for TKA projected to increase 673% by 2030^[1]. Occurring in tandem with this increase in demand is the exponential increase in obesity in society. Currently in Ireland, 36% of the population are overweight and 14% obese and this is estimated to increase further in the future^[2]. It is well established that obesity confers an increased risk for a number of medical conditions including ischaemic heart disease, diabetes and stroke^[3]. It has also been shown that obesity increases the risk of development of osteoarthritis, particularly in the knee, which has potential implications for the demand for TKA in the future^[4].

Obesity has a number of implications for surgery in general, but in particular for elective surgery such as TKA. Obesity is an independent risk factor for a number of perioperative complications including acute coronary syndrome, wound infection and urinary tract infection^[5]. The outcome of obese patients that undergo TKA as compared to non-obese patients is of particular interest. Currently the evidence is unclear with some studies indicating that obese patients achieve inferior outcomes^[6] with others showing equivalent functional outcome^[7,8].

The aim of this study was to assess the effect of body mass index (BMI) on functional outcome in primary total knee arthroplasty.

MATERIALS AND METHODS

Patients that underwent primary total replacement were identified from a prospectively collected joint registry at a single institution. Ethical approval was obtained for the establishment of the joint registry and for on going research. The joint registry is maintained by a full time clinical nurse specialist and all demographic and clinical information for each arthroplasty procedure performed at the institution is prospectively anonymously recorded. Two thousand one hundred and eighty patients were identified during the period 2007-2013. Demographic data including age and gender were collated for each patient. Body mass index (BMI) was calculated for each patient at pre-operative assessment using the standardised formula; weight in kilograms squared, divided by height in metres squared. Functional outcome scores, the Western Ontario and McMaster University Arthritis Index (WOMAC) and the Short Form 36 (SF-36) were collected pre-operatively and 6 mo post operatively. Complications including revision, superficial and deep infection, deep venous thrombosis (DVT) and pulmonary embolism (PE) were recorded prospectively in the postoperative period.

Patients were divided into two comparative groups for the purpose of the study, those with a normal BMI (less than or equal to 25) Group 1 and those who were overweight or obese (greater than 25) Group 2 according to the WHO BMI classification^[9]. A separate sub-group analysis was performed comparing all five WHO BMI groups; Normal weight, overweight, class 1 obese, class 2 obese and class 3 obese.

The Primary outcomes assessed were pre-operative and six-month post-operative WOMAC and the SF-36 scores. The WOMAC score is a validated self-administered questionnaire that assesses the condition of patients with hip and knee arthritis. It has a scale of 0 to 100, with a higher score equalling more pain, stiffness and functional limitation^[10]. The SF-36 is also a self-administered questionnaire that assesses quality of life. It has a scale of 0 to 100, with a higher score equating to a greater quality of life^[11]. Secondary outcomes assessed included

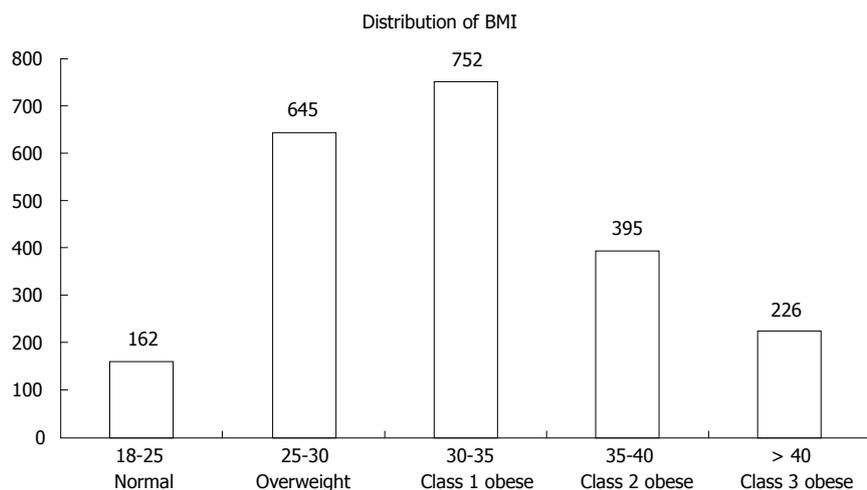


Figure 1 Distribution of patients according to World Health Organization body mass index classification. BMI: Body mass index.

Table 1 World Health Organization body mass index classification

WHO BMI classification	
Underweight	< 18.5
Normal range	18.5-25
Overweight	≥ 25
Obese	≥ 30
Class 1 obese	30-34.9
Class 2 obese	35-39.9
Class 3 obese	≥ 40

WTO: World Health Organization; BMI: Body mass index.

complications revision, superficial and deep infection, DVT and PE.

Statistical analysis

Statistical analysis was performed using STATA Version 12.1. All data was collated on a Microsoft Excel® (Microsoft Corporation, Seattle WA, United States) spreadsheet. Results were analyzed and are presented as mean, percentage and standard deviation for each BMI group according to the WHO classification as appropriate. Statistical significance between the main study groups (normal weight BMI < 25 vs BMI > 25) was assessed using the student *t* test, with significance set at *P* < 0.05.

Further sub-group analysis was performed comparing each of the WHO BMI sub-groups. Initially a One-way ANOVA analysis was performed to assess any difference between the groups. Further *post-hoc* Tukey HSD (honest significance test) analysis was then performed, comparing each of the sub-groups with significance set at *P* < 0.05. Statistical analysis was performed by Shane O'Neill MD.

RESULTS

A total of 2180 primary total knee replacements were performed at the institution between 2007 and 2013. The mean age was 67.9 years (28-92), with 36% Male and 64% Female. The mean follow up was 19.3 mo, with

Table 2 Pre- and post-operative functional outcome scores

	Group 1 (BMI < 25)	Group 2 (BMI > 25)	
WOMAC scores			
Pre-operative	52.7 (1-84)	53.7 (3-96)	<i>P</i> = 0.5
6 mo post-operative	29.7 (1-83)	27 (1-95)	<i>P</i> = 0.075
SF-36 Scores			
Pre-operative	48.8 (10.4-90.6)	48.25 (3.3-94.6)	<i>P</i> = 0.83
6 mo post-operative	61.34 (1-83)	62.15 (7.3-99.4)	<i>P</i> = 0.7

WOMAC: Western Ontario and McMaster University Arthritis Index; BMI: Body mass index.

a range of 6 mo to 5 years. The distribution according to BMI group is shown in Figure 1. The mean BMI was 31.9 (18-52) with 63% obese, 30% overweight and 7% normal weight. The two comparative study groups consisted of Group 1 (*n* = 162 patients) and Group 2 (*n* = 2018 patients).

Functional outcome

There was no significant difference in the pre-op WOMAC scores between Group 1; 52.7 (1-84) and Group 2; 53.7 (3-96) (*P* = 0.5). Similarly, there was no significant difference in the post op scores between the two groups, 29.7 (1-83) and 27 (1-95) (*P* = 0.075) respectively. There was no significant difference in either the pre-operative (*P* = 0.83) or post-operative (*P* = 0.7) SF-36 scores. The complete functional outcome scores are presented in Tables 1 and 2.

Sub-group analysis

Table 3 outlines 6-mo post operative functional scores arranged by WHO BMI sub-group in tabular format.

WOMAC: Initial One-way ANOVA analysis of the six-month post operative WOMAC scores between the 5 groups revealed a *P*-value < 0.01, suggesting a significant difference between one or more groups. Further *post-hoc* Tukey HSD testing revealed significant differences in the 6 mo postoperative WOMAC scores

Table 3 Sub-group analysis of post-operative functional outcome scores

	BMI < 25 Normal	BMI 25-29 Overweight	BMI 30-34 Class 1 obese	BMI 35-39 Class 2 obese	BMI > 40 Class 3 obese
WOMAC scores					
6 mo post-operative	29.67	25.8	25.5	30.8	28.6
SF-36 Scores					
6 mo post-operative	61.34	63.93	63.65	58.16	58.47

WOMAC: Western Ontario and McMaster University Arthritis Index; BMI: Body mass index.

comparing BMI 25-29 (overweight) 25.80 vs BMI 35-39 (class 2 obese) 30.80 ($P < 0.01$) and BMI 30-34 (class 1 obese) 25.50 vs BMI 35-39 (class 2 obese) 30.80 ($P < 0.01$). There was no significant difference in post operative WOMAC scores in the other BMI subgroup analysis.

SF-36: Initial One-way ANOVA analysis of the six month post operative SF-36 scores between the 5 groups revealed a P -value < 0.01 , suggesting a significant difference between one or more groups. Further post-hoc Tukey HSD Testing revealed significant differences in the six month postoperative SF-36 scores comparing BMI 25-29 (overweight) 63.93 vs BMI 35-39 (class 2 obese) 58.16 ($P < 0.01$) and BMI 30-34 (class 1 obese) 63.65 vs BMI 35-39 (class 2 obese) 58.16 ($P < 0.01$). There was no significant difference in post operative SF-36 scores in the other BMI sub-group analysis.

Complications

There were no complications in Group 1 ($n = 162$) at latest follow-up. There were 19 (0.87%) revisions, 32 (1.47%) superficial infections, 9 (0.41%) deep infections, 10 (0.46%) DVTs and 9 (0.41%) PEs in Group 2 ($n = 2018$) over the same mean follow-up. The absolute number of complications was not sufficient to perform a meaningful statistical analysis.

DISCUSSION

Overall the study revealed no significant difference in short-term post-operative functional outcome in patients with a normal BMI as compared to overweight or obese patients. Sub-group analysis found significantly lower functional outcome scores in class 2 obese patients (BMI 35-39.9) compared to both overweight and class 1 obese patient.

The study highlights that, the vast majority of patients now presenting to our institution for total knee replacement, 93% are either overweight or obese. This is significantly higher than the baseline levels in the general population, where 50% are either overweight or obese^[2]. This finding is mirrored in previous studies, which also revealed a considerable proportion of patients undergoing total knee arthroplasty are now obese^[12]. According to the latest National joint registry in the United Kingdom (NJR) figures (2013), the mean

BMI of patients undergoing TKA in the United Kingdom is now 30.8 (Class 1 obese)^[13]. This underlines the significant burden that this increase in BMI will place on orthopaedic services now and in the future.

The principle finding in this study of equivalent functional outcome comparing normal weight BMI < 25 individuals with BMI > 25 is in keeping with a recent study of 13673 primary total knee replacements by Baker *et al*^[14] using NJR data. They found that the improvement of patient reported outcomes (PROMs) were similar irrespective of BMI. Similarly, Desmukh *et al*^[15] revealed no correlation with BMI and functional outcome at 1 year. However, a consensus has yet to be reached in the literature, as there is also evidence that increasing BMI, particularly greater than 40 results in inferior clinical outcomes. Collins *et al*^[16] reviewed 445 total knee replacements and found inferior clinical outcome scores in individuals with a BMI greater than 30 at 9 years follow up. Interestingly, although obese patients achieved lower outcome scores as compared to non-obese patients, they achieved significant absolute functional improvement and the authors concluded that they "found no reason to limit access to total knee replacement in obese patients". While there was no difference in our main outcome measure, the sub-group analysis revealed significantly worse functional outcomes in the class 2 obese cohort compared to both the overweight and class 1 obese cohort. Interestingly the class 3 obese cohort did not demonstrate any significant difference in functional outcome scores. All cohorts achieved significant absolute improvements in functional outcome measures compared to preoperative values. The significance of our finding of inferior outcomes in the class 2 cohort is unclear. While we have included a relatively large cohort in this study (2180), perhaps larger numbers found in registry studies are necessary to define clear sub-group differences.

Despite no difference in functional outcome, the incidence of all complications was higher in the overweight and obese cohort as compared to the normal weight cohort. The evidence in the literature is clear in relation to the increased risk of perioperative complications with increasing BMI in TKA. The aetiology behind this is multifactorial. Wound healing and the development of both superficial and deep peri-prosthetic joint infections are significantly more common with increasing BMI. A recent meta-analysis

by Kerkhoffs *et al*^[17] revealed an odds ratio of 1.9 for all infection and 2.38 for deep infection in obese patients as compared to non-obese patients in an analysis of 15276 and 5061 patients respectively. Obese patients are also at a higher risk of thromboembolic disease post operatively^[18]. It is imperative that patients are counselled in detail regarding the increased risk of perioperative complications with increasing BMI. While it would seem intuitive that patients should attempt to lose weight prior to surgery, some recent evidence suggests that obese patients that lose a significant proportion of bodyweight preoperatively, actually have a higher rate of surgical site infection compared to control^[19]. Further research is needed in relation to perioperative weight management, however it raises interesting questions about the best way to manage this ever-expanding cohort of overweight and obese patients.

Due to the current demographics of our patient cohort, there were relatively few normal weight individuals presenting for surgery and therefore available for inclusion in the study. Similarly, larger studies using registry data may be necessary to elucidate clear sub-group differences. While the patient numbers were sufficient to statistically compare the functional outcome scores, there was an insufficient incidence of complications to draw any statistical conclusions in relation to complication differences. We acknowledge that early functional outcome may not correspond to long-term functional outcome and further research in this area is required.

In conclusion, overall there was no difference in early post-operative functional outcome comparing normal weight individuals with those of a BMI > 25 in a cohort of 2080 primary total knee replacements. Patients should be counselled regarding the potential increased risk of complications with increasing BMI, however they should not be denied TKA based solely on weight if medically fit to undergo the procedure.

COMMENTS

Background

The demand for total knee arthroplasty is increasing year on year and is projected to increase further in the future. Parallel to this the average weight of individuals is also increasing year on year. This directly corresponds to an increase in demand for total knee replacement (TKR), as increasing weight is associated with increased risk of symptomatic degenerative change in the knee. It is therefore imperative that the authors study the efficacy and safety of performing TKR on this patient cohort.

Research frontiers

The author's group perform high volume multi-surgeon arthroplasty at a single dedicated unit. This paper provides evidence for the efficacy for TKR in this patient cohort irrespective of body mass index (BMI).

Innovations and breakthroughs

Recent innovations in perioperative pain management and the enhanced recovery protocol have had a positive impact in decreasing length of stay and rehab potential for patients undergoing this procedure. This is particularly relevant to overweight and obese individuals for whom it imperative that they

mobilise early to try and minimise the risk of perioperative complications.

Applications

Patients with severe degenerative change affecting their quality of life and mobility can benefit from total knee arthroplasty. The procedure can transform a patient's life, relieving them of chronic pain and improving mobility.

Terminology

TKR involves the replacement of the worn surfaces of the distal femur and proximal tibia and replacement with prosthetic implants, which can be secured with or without cement.

Peer-review

This is an interesting clinical study concerning the effect of BMI on functional outcome and complications in primary total knee arthroplasty.

REFERENCES

- 1 **Kurtz S**, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89**: 780-785 [PMID: 17403800 DOI: 10.2106/JBJS.F.00222]
- 2 **Morgan KMH**, Watson D, Perry I, Barry M, Shelley E, Harrington J, Molcho M, Layte, RTN, van Lente E, Ward M, Lutomski J, Conroy R, Brugha R. SLAN 2007 Survey of lifestyle attitudes and nutrition in Ireland. Main Report. Dublin: Department of Health and Children, 2007
- 3 **Bray GA**. Overweight is risking fate. Definition, classification, prevalence, and risks. *Ann N Y Acad Sci* 1987; **499**: 14-28 [PMID: 3300479 DOI: 10.1111/j.1749-6632.1987.tb36194.x]
- 4 **Felson DT**, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med* 1988; **109**: 18-24 [PMID: 3377350 DOI: 10.7326/0003-4819-109-1-18]
- 5 **Bambade OA**, Rutter TW, Nafiu OO, Dorje P. Postoperative complications in obese and nonobese patients. *World J Surg* 2007; **31**: 556-560; discussion 561 [PMID: 16957821 DOI: 10.1007/s00268-006-0305-0]
- 6 **Foran JR**, Mont MA, Rajadhyaksha AD, Jones LC, Etienne G, Hungerford DS. Total knee arthroplasty in obese patients: a comparison with a matched control group. *J Arthroplasty* 2004; **19**: 817-824 [PMID: 15483795 DOI: 10.1016/j.arth.2004.03.017]
- 7 **Amin AK**, Patton JT, Cook RE, Brenkel IJ. Does obesity influence the clinical outcome at five years following total knee replacement for osteoarthritis? *J Bone Joint Surg Br* 2006; **88**: 335-340 [PMID: 16498007 DOI: 10.1302/0301-620X.88B3.16488]
- 8 **Spicer DD**, Pomeroy DL, Badenhansen WE, Schaper LA, Curry JI, Suthers KE, Smith MW. Body mass index as a predictor of outcome in total knee replacement. *Int Orthop* 2001; **25**: 246-249 [PMID: 11561501 DOI: 10.1007/s002640100255]
- 9 **WHO**. Global database on Body Mass Index: BMI Classification. Geneva: World Health Organization, 2006
- 10 **WOMAC Osteoarthritis Index User Guide**. Version V. Australia: Brisbane, 2002
- 11 **Ware JE**, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473-483 [PMID: 1593914 DOI: 10.1097/00005650-199206000-00002]
- 12 **Kremers HM**, Visscher SL, Kremers WK, Naessens JM, Lewallen DG. The effect of obesity on direct medical costs in total knee arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 718-724 [PMID: 24806008 DOI: 10.2106/JBJS.M.00819]
- 13 **National Joint Registry**. National Joint Registry Annual Report, 2014. Available from: URL:<http://www.hqip.org.uk/resources/national-joint-registry-annual-report-2014/>
- 14 **Baker P**, Petheram T, Jameson S, Reed M, Gregg P, Deehan D. The association between body mass index and the outcomes of total knee arthroplasty. *J Bone Joint Surg Am* 2012; **94**: 1501-1508

[PMID: 22992819 DOI: 10.2106/JBJS.K.01180]

- 15 **Deshmukh RG**, Hayes JH, Pinder IM. Does body weight influence outcome after total knee arthroplasty? A 1-year analysis. *J Arthroplasty* 2002; **17**: 315-319 [PMID: 11938508 DOI: 10.1054/arth.2002.30776]
- 16 **Collins RA**, Walmsley PJ, Amin AK, Brenkel IJ, Clayton RA. Does obesity influence clinical outcome at nine years following total knee replacement? *J Bone Joint Surg Br* 2012; **94**: 1351-1355 [PMID: 23015559 DOI: 10.1302/0301-620X.94B10.28894]
- 17 **Kerkhoffs GM**, Servien E, Dunn W, Dahm D, Bramer JA, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. *J Bone Joint Surg Am* 2012; **94**: 1839-1844 [PMID: 23079875 DOI: 10.2106/JBJS.K.00820]
- 18 **Mantilla CB**, Horlocker TT, Schroeder DR. Risk factors for clinically relevant pulmonary embolism and deep venous thrombosis in patients undergoing primary hip or knee arthroplasty. *Anesthesiology* 2003; **99**: 552-560 [PMID: 12960538]
- 19 **Inacio MC**, Kritz-Silverstein D, Raman R, Macera CA, Nichols JF, Shaffer RA, Fithian DC. The risk of surgical site infection and re-admission in obese patients undergoing total joint replacement who lose weight before surgery and keep it off post-operatively. *Bone Joint J* 2014; **96-B**: 629-635 [PMID: 24788497 DOI: 10.1302/0301-620X.96B5.33136]

P- Reviewer: Cui QT, De Fine M, Drosos GI, Fernandez-Fairen M, Hasegawa M **S- Editor:** Qiu S **L- Editor:** A **E- Editor:** Lu YJ



Retrospective Study

Outcome of repair of chronic tear of the pectoralis major using corkscrew suture anchors by box suture sliding technique

Deepak Joshi, Jitesh Kumar Jain, Deepak Chaudhary, Utkarsh Singh, Vineet Jain, Ajay Lal

Deepak Joshi, Jitesh Kumar Jain, Deepak Chaudhary, Utkarsh Singh, Sports Injury Centre, Safdarjung Hospital, New Delhi 110029, India

Vineet Jain, Ajay Lal, Sports Injury Centre, Safdarjung Hospital and Vardhman Mahavir Medical College, New Delhi 110029, India

Author contributions: Joshi D and Chaudhary D are the chief surgeon who performed all surgeries; Singh U and Jain V assisted the surgery and helped in data collection; Jain JK drafted the manuscript; Lal A did the statistical work.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the sports injury centre, Safdarjung Hospital, New Delhi.

Informed consent statement: Informed consent was obtained from all individual participants included in the study.

Conflict-of-interest statement: All authors declare that they have no financial relationship to disclose.

Data sharing statement: No additional data available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Jitesh Kumar Jain, MS, Sports Injury Centre, Safdarjung Hospital, Ansari Nagar, New Delhi 110029, India. dr.jiteshajmera@yahoo.com
Telephone: +91-96-43966494

Received: March 23, 2016

Peer-review started: March 24, 2016

First decision: May 16, 2016

Revised: June 18, 2016

Accepted: July 29, 2016

Article in press: August 1, 2016

Published online: October 18, 2016

Abstract

AIM

To assess the functional and clinical results of repair of chronic tears of pectoralis major using corkscrew and sliding suture technique.

METHODS

In this retrospective study, we reviewed the results of pectoralis major repair in 11 chronic cases (> 6 wk) done between September 2011 and December 2014 at our institute. In all cases repair was done by same surgeon using corkscrew suture anchors and box suture sliding technique. At 6 mo, after surgery magnetic resonance imaging was done to see the integrity of the repair. Functional evaluation was done using Penn and ASES scores. Pre and postoperative Isokinetic strength was measured.

RESULTS

Average follow-up was 48.27 ± 21.0 mo. The Wilcoxon signed rank test was used to evaluate the outcome scores. The average ASES score increased from an average of 54.63 ± 13.0 preoperatively to 95.09 ± 2.60 after surgery at their last follow-up. The average Penn score also increased from 5.72 ± 0.78 , 2.81 ± 1.32 and 45.81 ± 1.72 to 9.36 ± 0.80 , 8.27 ± 0.90 and 59 ± 1.34 for pain, satisfaction and function respectively. Follow up magnetic resonance imaging (MRI) (at 6 mo) showed continuity and the bulk of pectoralis major muscle in all cases. Average isokinetic strength deficiency in horizontal

adduction at 60° was 13.63% ± 6.93% and at 120° was 10.18% ± 4.93% and in flexion at 60° was 10.72% ± 5.08% and at 120° was 6.63% + 3.74%. Results showed that both ASES and Penn score improved significantly (2 tailed *P* value = 0.0036).

CONCLUSION

We could conclude from this series that pectoralis major repair even in chronic cases using 5.5 mm corkscrew anchors give excellent functional and cosmetic results. In chronic cases the repairable length of the tendon is not available and sliding suture technique allows for fixation of worn out tendomuscular junction to bone without letting cutting through the muscle.

Key words: Pectoralis major tear; Corkscrew suture anchors; Chronic tears; Bench press; Tendon repair

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We are presenting the results of repair of rare chronic tears of pectoralis major. This is one of the longest series of repair of chronic pectoralis major tears by corkscrew suture anchors with midterm follow-up. In chronic tears hardly any repairable length of the tendon is available and what available is largely musculotendinous unit. We used a new technique to prevent cutting through of sutures from retracted musculotendinous unit in chronic tears. We have obtained excellent results with this technique.

Joshi D, Jain JK, Chaudhary D, Singh U, Jain V, Lal A. Outcome of repair of chronic tear of the pectoralis major using corkscrew suture anchors by box suture sliding technique. *World J Orthop* 2016; 7(10): 670-677 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/670.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.670>

INTRODUCTION

Pectoralis major tear is a relatively rare and extremely traumatic orthopedic injury. Recently there has been an increase in reporting of such cases, especially in young, athletic males between 20 to 40 years of age, who are into body building or weightlifting sports^[1]. Pectoralis major muscle has 2 heads of origin, sternocostal and clavicular. Sternocostal part forms the deeper posterior lamina and inserts more proximally on humerus and clavicular part forms the anterior lamina and inserts distally. Sternocostal part primarily internally rotates and adducts the shoulder whereas clavicular part forward flexes and adducts the shoulder. Traditionally, pectoralis major tear were being managed conservatively, but recently the surgical management of pectoralis major repair especially in young athletes has been recommended^[2]. Cases of repair of both acute and

chronic tear of pectoralis major have been reported. Tietjen^[3] classified these injuries into three classes: (1) sprain; (2) partial tear; and (3) complete tear. Complete tear is further classified into tear of (1) muscle origin; (2) muscle belly; (3) musculotendinous junction and of tendon itself (4) recently, two more subclasses have been added^[4-8]; (5) bony flake avulsion of the tendon; and (6) intratendinous ruptures. Chronic tears of pectoralis major are different from acute tears as the repairable length of the tendon is hardly available for fixation. This makes fixation difficult as cutting through the retracted musculo-tendinous junction of sutures is likely. This led us to develop a new technique which resulted in excellent results in chronic cases of this rare injury.

In this article we are reporting our experience of repair of chronic tendon rupture of pectoralis major muscles in 11 cases where we assessed clinical, functional and cosmetic results and incidence of re-rupture.

MATERIALS AND METHODS

In this retrospective study, we reviewed the results of the pectoralis major repair in 11 cases (Table 1) done between September 2011 and December 2014 at our institute. The inclusion criteria were all chronic cases (> 6 wk) of pectoralis major tear repair who had minimum 2-year follow up with the availability of all medical records. All patients presented with common complaints of weakness of involved shoulder and loss of shape/bulge of axillary border. All cases felt sudden tearing sensation and pain in the axilla at time of injury. This was followed by development of bruises and swelling in the axilla. All were managed conservatively for at least 6 wk by local practitioner before presentation (range 1.5-4 mo). On examination, there was a weakness of adduction and internal rotation strength on the involved side compared to the other side and there was a loss of the anterior axillary fold (Figure 1). No patient gave a history of the use of anabolic steroids or any local injections. Diagnosis was confirmed by radiologist in all cases on MRI scan. Multi-planar coronal oblique and axial scans (T2-weighted fat-suppressed and proton density-weighted fat-suppressed images) were taken in all cases. Interstitial edema, retracted tendons and tear with fluid signal were considered positive findings to make the diagnosis. All patients were managed surgically.

Patients were followed up at 2, 6, 12 and 24 wk and subsequently at 3 monthly intervals and assessed clinically by range of motion and strength measurement. After surgery, shoulder was immobilized in a sling for 3 wk. Passive forward flexion and abduction were started after 2 wk. External rotation was restricted to 15 degrees in 1st 6 wk. Range of motion was gradually increased to achieve full range of motion by 3 mo. Strengthening exercises were started by the end of 2 mo and gradually increased from isometric exercises to

Table 1 Details of patients and functional assessment

S/N Profession	Age/sex	Mode of injury	Type of tear	Time between injury and surgery	Follow up	ROM	Penn Score pre surgery	Penn Score (at final follow up)	ASES		Cosmetic appearance
									Pre-surgery	Post-surgery	
1 Student	24/M	Bench press, 190 kg	Both heads avulsion at bony insertion on the humerus	4 mo	82 mo	Full	Pain-6 Satisfaction-3 Function-45	Pain-10 Satisfaction-9 Function-60	40	98.33	No complaints
2 Wrestler	25/M	Bench press, 180 kg	Sternal head avulsion at bony insertion on humerus	3 mo	80 mo	Full	Pain-5 Satisfaction-4 Function-46	Pain-10 Satisfaction-9 Function-60	43.33	98.33	No complaints
3 Gym trainer	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	3 mo	68 mo	Full	Pain-7 Satisfaction-3 Function-44	Pain-9 Satisfaction-9 Function-58	45	91.66	No complaints
4 Kabaddi player	25/M	While playing Kabaddi (Forceful abduction and extension)	Both heads avulsion at bony insertion on the humerus	1.5 mo	56 mo	Full	Pain-6 Satisfaction-3 Function-45	Pain-8 Satisfaction-7 Function-58	42.77	96.1	No complaints
5 Wrestler	30/ M	Bench press, 150 kg	Both heads avulsion at bony insertion on the humerus	3 mo	50 mo	Full	Pain-5 Satisfaction-3 Function-45	Pain-8 Satisfaction-7 Function-56	40	91.66	Not fully satisfied with cosmetic appearance (Changed profession due to pain in carrying weight)
6 Wrestler	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	2 mo	44 mo	Full	Pain-6 Satisfaction-3 Function-45	Pain-9 Satisfaction-8 Function-60	68.32	93.33	No complaints
7 Weightlifter	25/M	Bench press, 170 kg	Sternal head avulsion at bony insertion on humerus	3 mo	40 mo	Full	Pain-6 Satisfaction-3 Function-45	Pain-9 Satisfaction-7 Function-60	78.32	98.33	Not fully satisfied with cosmetic appearance
8 Wrestler	28/M	While wrestling	Both heads avulsion at bony insertion on the humerus	2 mo	32 mo	Full	Pain-4 Satisfaction-0 Function-44	Pain-10 Satisfaction-8 Function-58	61.66	95	No complaints
9 Weightlifter	20/M	Bench press 165 kg	Sternal head avulsion at bony insertion on humerus	1.5 mo	30 mo	Full	Pain-6 Satisfaction-3 Function-48	Pain-10 Satisfaction-9 Function-59	63.31	93.33	No complaints
10 Student	27/M	Bench press	Sternal head avulsion at bony insertion on humerus	3.5 mo	25 mo	Full	Pain-6 Satisfaction-5 Function-48	Pain-10 Satisfaction-9 Function-60	61.64	98.33	No complaints
11 Weightlifter	23/M	Bench press 160 kg	Sternal head avulsion at bony insertion on humerus	2 mo	24 mo	Full	Pain-6 Satisfaction-1 Function-49	Pain-10 Satisfaction-9 Function-60	56.66	96.66	No complaints

M: Male; F: Female.

isotonic exercises. Postoperatively results were assessed by American shoulder and elbow assessment (ASES) score, Penn scores and bilateral isokinetic strength testing by Humac™ (CSMI, Stoughton, MA). Deficit in strength was calculated as the percent difference between the higher and lower peak torque of the two limbs divided by the highest peak torque at 60 degrees

and 120 degrees. The Wilcoxon signed rank test was used to assess the difference in pre and post-operative ASES and Penn scores and isometric strength.

Surgical technique

Patients were operated in the beach chair position. An incision of 5 cm was given in distal part of deltopectoral



Figure 1 Preoperative physical appearance with loss of anterior axillary fold (black arrow).

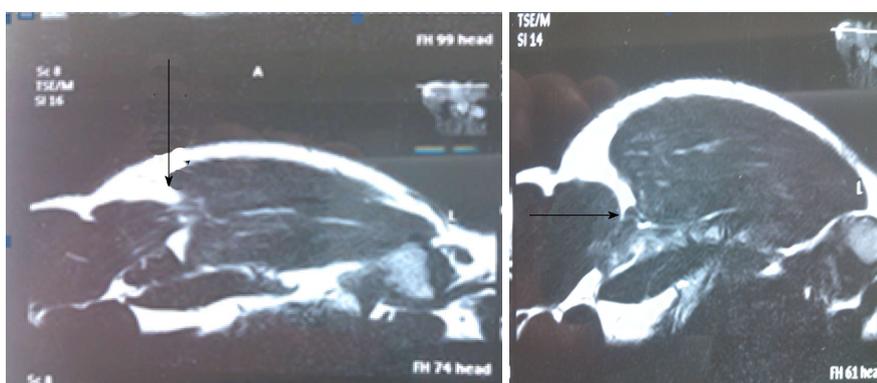


Figure 2 Magnetic resonance imaging report showing near complete tear (arrow) of Pectoralis major muscle.

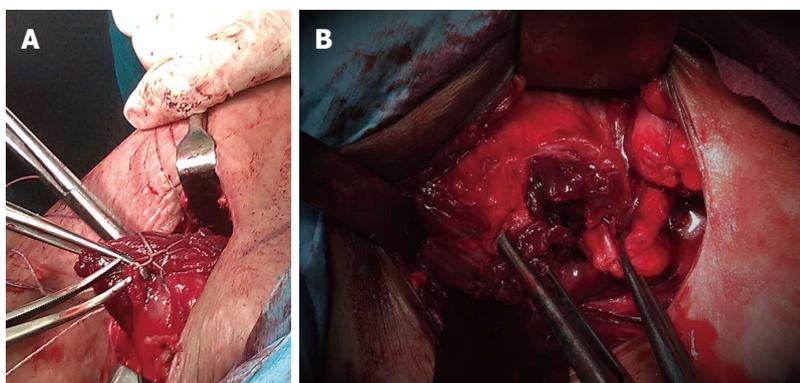


Figure 3 Torn pectoralis major tendon Sternal head identified and whip sutured (A); and a complete tear of both sternal and clavicular heads, held separately with forceps after mobilization (B).

groove. Torn tendon of pectoralis major was identified and mobilized (Figures 2 and 3). The lateral lip of bicipital groove was exposed and its base was roughened with a rasp and drilling. Two double loaded 5.5 mm corkscrew anchors (Arthrex, Naples, United States) were deployed into the lateral lip proximally and distally at the insertion site of the tendon (Figure 4). Pectoralis major tendon was then attached to the lateral lip of bicipital groove with the help of anchors. The suturing was done in a box like fashion in the musculotendinous area to have a broader fixation and sliding knots followed by the half hitches were applied

with post being the free thread (not through the muscle tendon). This brings the broad bulk of muscular tissue in approximation to the insertion site. The technique (box suture-sliding technique, Figure 5) holds good for these types of chronic cases where the torn tendon often gets attrition and it is difficult to achieve secure fixation in the worn out tendon.

RESULTS

All patients were young and active (mean age 25.54 ± 2.60 years). Mean follow up was 48.27 ± 21.0 mo.

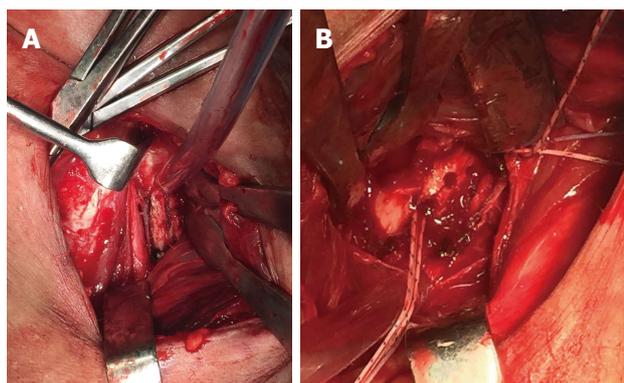


Figure 4 Exposure of bicipital groove (A), Biceps tendon is protected. Corkscrew anchors (double loaded) are deployed into the lateral lip of bicipital groove (B).

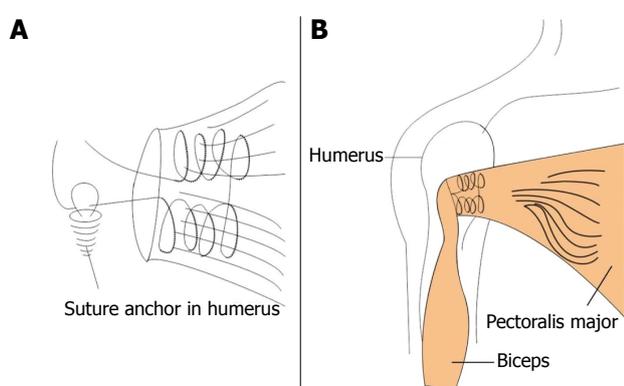


Figure 5 Box sliding technique. Musculotendinous unit was whipstitched (this makes like a box covering the broad area of delicate muscle to prevent cutting through the musculotendinous unit) and sliding Nikky's knot was used to push the tendon to bone (A). A final picture after the torn tendon has been secured to the lateral lip of bicipital groove with anchors (B).

Mean time from injury to surgery was 2.59 ± 0.83 mo. Nine cases sustained injury while doing bench press exercise in the gymnasium, one patient sustained injury while playing Kabaddi (A popular contact sport in South Asia) and one patient while wrestling. MRI showed near complete tear of the pectoralis major at axillary fold level in four cases and tear of Sternal head in seven cases (Figure 2).

All patients achieved their pre injury exercise level in gymnasium between 9 and 12 mo postoperatively and returned to their previous occupation except one patient (wrestler) who changed the profession due to pain in overhead activity and difficulty in carrying weight. All patients were happy with the cosmetic result regarding the appearance of axillary fold, compared to the other side (Figure 6C) except two patients. At 6 mo, all cases were able to do bench press with minimum 70 kg weight. There was no complication till last follow up. No patient suffered re-tear of the repair till last follow-up.

The average ASES score increased from an average of 54.63 ± 13.0 preoperatively to 95.09 ± 2.60 after

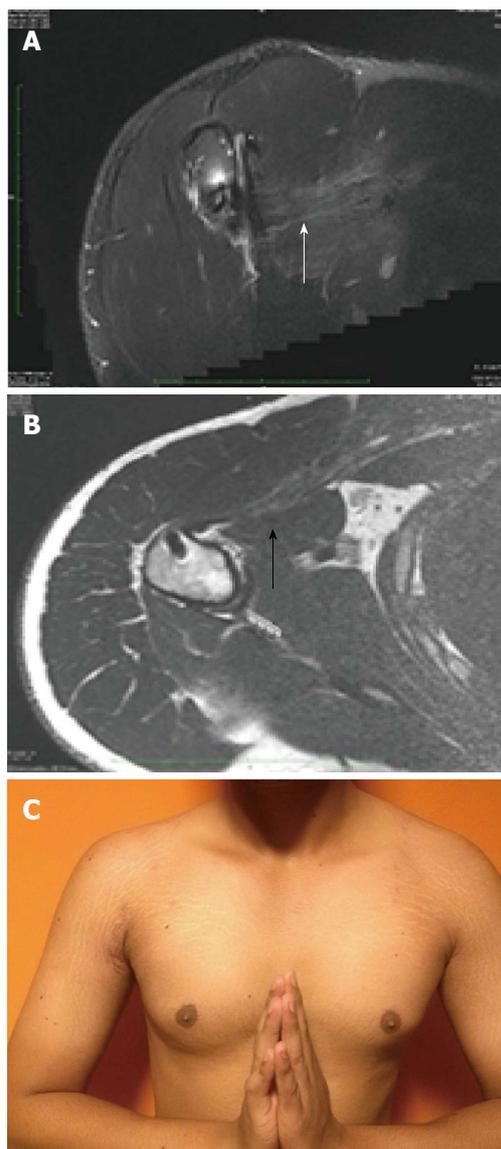


Figure 6 Magnetic resonance imaging at 6 mo follow up showing excellent continuity (arrow) and the bulk of pectoralis major muscle after repair (A, B); restoration of the anterior axillary fold after surgery (C).

surgery at their last follow-up. The average Penn score also increased from 5.72 ± 0.78 , 2.81 ± 1.32 and 45.81 ± 1.72 to 9.36 ± 0.80 , 8.27 ± 0.90 and 59 ± 1.34 for pain, satisfaction and function respectively. Follow up MRI (at 6 mo) showed continuity and the bulk of pectoralis major muscle in all cases (Figure 6A and B). Average isokinetic strength deficiency in horizontal adduction at 60° was $13.63\% \pm 6.93\%$ and at 120° was $10.18\% \pm 4.93\%$ and in flexion at 60° was $10.72\% \pm 5.08\%$ and at 120° was $6.63\% \pm 3.74\%$.

Statistical analysis: The Wilcoxon signed rank test was used to assess the difference in pre and post-operative ASES and Penn scores and isometric strength. Improvement in ASES score and all components of Penn scores were significant (Two tailed $P = 0.0036$, $P < 0.05$).

DISCUSSION

Athletes usually sustain pectoralis major injury as a result of violent, eccentric contraction of the muscle during athletic activities. Sudden forceful abduction and external rotation of contracted muscle is the usual mode of injury. Bench-pressing weights has been reported as the most common mode of injury^[4,8]. Other common modes of injury include rugby, football, wrestling and water skiing^[5-7]. Type III D (tendon tear) tear is the most common with a rate of 65%, followed by the type III C tears^[8]. To date just over 60 articles and 350 cases have been reported in English literature^[9]. Although first case was reported in 1822 more than 75% cases have been reported in last 20 years^[9]. This simply reflects the advancement of diagnostic modalities and our understanding of these injuries. Use of anabolic steroids has been reported as a risk factor in weightlifters in such cases^[10]. Sternocostal part stretches when the arm is abducted, externally rotated and extended and it fails more often before the clavicular part^[11].

Wolf *et al*^[11] in a cadaveric study showed that lower fibers of the sternocostal part are disproportionately lengthened and stressed in the last 30 degrees of extension. This explains why sternocostal part ruptures more often and before clavicular part. Females are less commonly exposed to high velocity sports and high end muscle building exercises. In addition to this larger tendon to muscle diameter in women has also been suggested^[12] for almost no incidence of pectoralis major tear in females.

Since the reporting of the 1st case of pectoralis major muscle tear by Patissier^[13] in 1822 its treatment has evolved from conservative to surgical management. Now most of the tears are treated surgically except for tears in elderly patients, those with sedentary lifestyles and minor muscle belly rupture^[7,14]. While conservative treatment has shown poor results^[15,16] surgical treatment has produced excellent outcomes^[7,8,13,15] and is the preferred treatment now. In a large series of surgical repair of pectoralis major tear, Aärimaa *et al*^[12] showed that early surgical repair has better outcomes than delayed repair. Eight weeks have been reported as an ideal time for surgery of pectoralis major tear^[15]. Patients who are treated conservatively show good relief in pain and achieve range of motion compared to surgically treat patients, but they fail to achieve their pre injury level of functional strength and have cosmetic deformity. Surgical management usually involves reattachment of the tendon to humerus by drill holes and tying sutures over a bone bridge^[15] anchors^[16-25], and staples^[23]. Three main techniques of re-attachment of tendon to humerus are bone tunnel technique, bone trough technique and suture anchor technique. In bone tunnel technique sutures are passed using a curved suture passer through curved/angled bone tunnels and tendon are tied over a bone bridge reattaching the tendon to humerus. In bone trough technique drill holes are made into the bone trough at the site of tendon



Figure 7 In acute cases reparable length of the tendon may be available for repair, but in chronic cases it is mainly muscle, which remains available to be attached back to the bone (Figure 3).

insertion. Suture anchors are being increasingly used in recent years, probably due to increasing familiarity of surgeons with these anchors and almost all the case series of repair with suture anchors have been reported after 2004^[2,17-19,25]. Care should be taken not to injure the biceps tendon while making trough or drill holes in the bicipital groove.

Due to the rarity of injury no fixation method has been reported to give superior results compared to other methods, however drill holes fixation with or without trough remain the most common method of repair in most of the reported case series. Recently few cadaveric studies have given the results of biomechanical studies of common methods of pectoralis major repair. Sherman *et al*^[21] and Hart *et al*^[22] concluded that suture anchor repair and trans osseous repair of pectoralis major confer the same biomechanical integrity, whereas Rabuck *et al*^[20] found a bone trough repair of the pectoralis major tendon was stronger than suture anchor repair. More studies are needed to reach a conclusion to recommend one method over another. We used suture anchors to fix the tendon to bone as these are easy to use and give firm anchorage in hard young cortical bone.

Although, excellent results have been reported in most cases of late presentation, the main differences in management of acute and chronic cases from the surgery point of view, is the available length of the tendon for repair. In a cadaveric study at our centre (unpublished data) we have seen that the approximate length of pectoralis major tendon from musculotendinous junction is 2.5 cm (Figure 7). In chronic cases the reparable length of the tendon is hardly available and it is mostly muscle/musculotendinous junction, which is anchored to bone (Figure 3). In our technique we used sliding knot, to prevent cutting through of suture through the muscle. Tendon mobilization may be a problem in chronic cases due to adhesions and scars. After incision of these peri-tendinous adhesions it may be possible to bring the tendon to the insertion site at humerus without tension^[2]. If the sufficient excursion of the tendon is not possible use of allograft or autograft is necessary^[24]. In our series we did not find any difficulty in the mobilization

and fixation of pectoralis major tendon by corkscrew anchors and achieved excellent results.

The only limitation of this study is that the sample size is small, but due to the rarity of the tear of pectoralis major, results are worth reporting. As such, few cases of chronic tears have been reported and there is no consensus for a surgical repair method for chronic tears. We could conclude from this series that pectoralis major repair can be done even in chronic cases using 5.5 mm corkscrew anchors and it gives excellent functional and cosmetic results. Surgery should be done in all such active persons who want to get back to pre-injury activity level.

COMMENTS

Background

Pectoralis major tears are rare injuries with reporting of just over 350 cases in English literature. Pectoralis major muscle has 2 heads of origin, sternocostal and clavicular. The Sternocostal part is mainly internal rotator and adductor of the shoulder whereas the clavicular part is mainly forward flexor and adductor of the shoulder. Management of these tears has been changed over the years from conservative to surgical and now most of the pectoralis major tears are being managed surgically, especially in young athletes. Tears are classified into sprain, partial and complete tears. The most common type of complete tears are tears of tendon itself and tears at musculotendinous junction. Many surgical repair methods have been published for both acute and chronic cases with no published reports of superiority of one method over others.

Research frontiers

In chronic retracted tear of the pectoralis major muscle, repairable length of the tendon is hardly available and mostly it is the musculotendinous unit which remains left. In these cases cutting of suture through the retracted musculotendinous unit is likely while pulling it towards the humerus. To overcome this difficulty the authors used specially designed box suture sliding technique with corkscrews.

Innovation and breakthrough

Sliding knots with suture anchors are commonly used in arthroscopic surgeries. Their study describes the useful role of sliding knot and corkscrew suture anchors in repair of chronic tears of pectoralis major muscle.

Application

The results of this study describe the valuable role of corkscrew suture anchors and sliding knot in repair of chronic tears of the pectoralis major.

Peer-review

The authors of this paper evaluated the results of repair of chronic tears of the pectoralis major muscle using corkscrews and a specially devised sliding knot in 11 patients. They obtained excellent results with significant improvement in ASES score, Penn score and isokinetic strength testing.

REFERENCES

- 1 **Potter BK**, Lehman RA, Doukas WC. Pectoralis major ruptures. *Am J Orthop* (Belle Mead NJ) 2006; **35**: 189-195 [PMID: 16689519]
- 2 **Petilon J**, Carr DR, Sekiya JK, Unger DV. Pectoralis major muscle injuries: evaluation and management. *J Am Acad Orthop Surg* 2005; **13**: 59-68 [PMID: 15712983 DOI: 10.5435/00124635-200501000-00008]
- 3 **Tietjen R**. Closed injuries of the pectoralis major muscle. *J Trauma* 1980; **20**: 262-264 [PMID: 7359604 DOI: 10.1097/00005373-198003000-00015]
- 4 **Hasegawa K**, Schofer JM. Rupture of the pectoralis major: a case report and review. *J Emerg Med* 2010; **38**: 196-200 [PMID: 18818044 DOI: 10.1016/j.jemermed.2008.01.025]
- 5 **Hanna CM**, Glenny AB, Stanley SN, Caughey MA. Pectoralis major tears: comparison of surgical and conservative treatment. *Br J Sports Med* 2001; **35**: 202-206 [PMID: 11375884 DOI: 10.1136/bjism.35.3.202]
- 6 **Connell DA**, Potter HG, Sherman MF, Wickiewicz TL. Injuries of the pectoralis major muscle: evaluation with MR imaging. *Radiology* 1999; **210**: 785-791 [PMID: 10207482 DOI: 10.1148/radiology.210.3.r99fe43785]
- 7 **Schepesis AA**, Grafe MW, Jones HP, Lemos MJ. Rupture of the pectoralis major muscle. Outcome after repair of acute and chronic injuries. *Am J Sports Med* 2000; **28**: 9-15 [PMID: 10653537]
- 8 **Bak K**, Cameron EA, Henderson IJ. Rupture of the pectoralis major: a meta-analysis of 112 cases. *Knee Surg Sports Traumatol Arthrosc* 2000; **8**: 113-119 [PMID: 10795675 DOI: 10.1007/s001670050197]
- 9 **ElMaraghy AW**, Devereaux MW. A systematic review and comprehensive classification of pectoralis major tears. *J Shoulder Elbow Surg* 2012; **21**: 412-422 [PMID: 21831661 DOI: 10.1016/j.jse.2011.04.035]
- 10 **März J**, Novotný P. [Pectoralis major tendon rupture and anabolic steroids in anamnesis--a case review]. *Rozhl Chir* 2008; **87**: 380-383 [PMID: 18810933]
- 11 **Wolfe SW**, Wickiewicz TL, Cavanaugh JT. Ruptures of the pectoralis major muscle. An anatomic and clinical analysis. *Am J Sports Med* 1992; **20**: 587-593 [PMID: 1443329 DOI: 10.1177/036354659202000517]
- 12 **Aärimaa V**, Rantanen J, Heikkilä J, Helttula I, Orava S. Rupture of the pectoralis major muscle. *Am J Sports Med* 2004; **32**: 1256-1262 [PMID: 15262651 DOI: 10.1177/0363546503261137]
- 13 **Patissier P**. Traite des maladies des artisans. *Paris* 1882; **2**: 162-164
- 14 **Beloosesky Y**, Grinblat J, Weiss A, Rosenberg PH, Weisbort M, Hendl D. Pectoralis major rupture in elderly patients: a clinical study of 13 patients. *Clin Orthop Relat Res* 2003; **(413)**: 164-169 [PMID: 12897606 DOI: 10.1097/01.blo.0000076803.53006.12]
- 15 **Kretzler HH**, Richardson AB. Rupture of the pectoralis major muscle. *Am J Sports Med* 1989; **17**: 453-458 [PMID: 2782527 DOI: 10.1177/036354658901700401]
- 16 **de Castro Pochini A**, Ejnisman B, Andreoli CV, Monteiro GC, Silva AC, Cohen M, Albertoni WM. Pectoralis major muscle rupture in athletes: a prospective study. *Am J Sports Med* 2010; **38**: 92-98 [PMID: 19880715 DOI: 10.1177/0363546509347995]
- 17 **Merolla G**, Campi F, Paladini P, Porcellini G. Surgical approach to acute pectoralis major tendon rupture. *G Chir* 2009; **30**: 53-57 [PMID: 19272235]
- 18 **Kakwani RG**, Matthews JJ, Kumar KM, Pimpalnerkar A, Mohtadi N. Rupture of the pectoralis major muscle: surgical treatment in athletes. *Int Orthop* 2007; **31**: 159-163 [PMID: 16847645 DOI: 10.1007/s00264-006-0171-2]
- 19 **Samitier GS**, Marciano AI, Farmer KW. Pectoralis major transosseous equivalent repair with knotless anchors: Technical note and literature review. *Int J Shoulder Surg* 2015; **9**: 20-23 [PMID: 25709241 DOI: 10.4103/0973-6042.150219]
- 20 **Rabuck SJ**, Lynch JL, Guo X, Zhang LQ, Edwards SL, Nuber GW, Saltzman MD. Biomechanical comparison of 3 methods to repair pectoralis major ruptures. *Am J Sports Med* 2012; **40**: 1635-1640 [PMID: 22679296 DOI: 10.1177/0363546512449291]
- 21 **Sherman SL**, Lin EC, Verma NN, Mather RC, Gregory JM, Dishkin J, Harwood DP, Wang VM, Shewman EF, Cole BJ, Romeo AA. Biomechanical analysis of the pectoralis major tendon and comparison of techniques for tendo-osseous repair. *Am J Sports Med* 2012; **40**: 1887-1894 [PMID: 22781500 DOI: 10.1177/0363546512452849]
- 22 **Hart ND**, Lindsey DP, McAdams TR. Pectoralis major tendon rupture: a biomechanical analysis of repair techniques. *J Orthop Res* 2011; **29**: 1783-1787 [PMID: 21538507 DOI: 10.1002/jor.21438]
- 23 **Egan TM**, Hall H. Avulsion of the pectoralis major tendon in a weight lifter: repair using a barbed staple. *Can J Surg* 1987; **30**:

- 434-435 [PMID: 3664412]
- 24 **Zafra M**, Muñoz F, Carpintero P. Chronic rupture of the pectoralis major muscle: report of two cases. *Acta Orthop Belg* 2005; **71**: 107-110 [PMID: 15792217]
- 25 **Mooers BR**, Westermann RW, Wolf BR. Outcomes Following Suture-Anchor Repair of Pectoralis Major Tears: A Case Series and Review of the Literature. *Iowa Orthop J* 2015; **35**: 8-12 [PMID: 26361438]

P- Reviewer: Fernandez-Fairen M, Madadi F **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Lu YJ



Observational Study

Is there a weekend effect in hip fracture patients presenting to a United Kingdom teaching hospital?

John Abraham Mathews, Madhavi Vindlacheruvu, Vikas Khanduja

John Abraham Mathews, Madhavi Vindlacheruvu, Vikas Khanduja, Department of Orthopaedics, Addenbrooke's Hospital, Cambridge CB2 0QQ, United Kingdom

Author contributions: Mathews JA, Vindlacheruvu M and Khanduja V contributed to study conception and design, as well as analysis and data interpretation; all contributed to editing, reviewing and final approval of the article.

Institutional review board statement: The National Hip Fracture Database has ethical approval by the NHS England HRA Confidentiality Advisory Group (CAG) to collect patient data without consent under Section 251 exemption (this approval was formerly administered under the NIGB-ECC/PIAG).

Informed consent statement: The National Hip Fracture Database is approved by the NHS England HRA Confidentiality Advisory Group (CAG) to collect patient data without consent under Section 251 exemption (this approval was formerly administered under the NIGB-ECC/PIAG).

Conflict-of-interest statement: None of the authors have any conflicting interests to declare (including but not limited to commercial, personal, political, intellectual or religious interests).

Data sharing statement: Technical appendix, statistical code, and dataset available from corresponding author at vikaskhanduja@aol.com. Ethical approval was not obtained to collect data without consent under Section 251 exemption. The presented data are anonymised and the risk of identification is negligible.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Vikas Khanduja, FRCS (Orth), Consultant

Surgeon, Department of Orthopaedics, Addenbrooke's Hospital, Hills Road, Cambridge CB2 0QQ, United Kingdom. vikaskhanduja@aol.com
Telephone: +44-1223-245151

Received: March 1, 2016
Peer-review started: March 1, 2016
First decision: March 21, 2016
Revised: July 29, 2016
Accepted: August 17, 2016
Article in press: August 18, 2016
Published online: October 18, 2016

Abstract

AIM

To compare mortality and time-to-surgery of patients admitted with hip fracture to our teaching hospital on weekdays vs weekends.

METHODS

Data was prospectively collected and retrospectively analysed for 816 hip fracture patients. Multivariate logistic regression was carried out on 3 binary outcomes (time-to-surgery < 36 h; 30-d mortality; 120-d mortality), using the explanatory variables time-of-admission; age; gender; American Society of Anesthesiologist (ASA) grade; abbreviated mental test score (AMTS); fracture type; accommodation admitted from; walking ability outdoors; accompaniment outdoors and season.

RESULTS

Baseline characteristics were not statistically different between those admitted on weekdays vs weekends. Weekend admission was not associated with an increased time-to-surgery ($P = 0.975$), 30-d mortality ($P = 0.842$) or 120-d mortality ($P = 0.425$). Gender ($P = 0.028$), ASA grade ($P < 0.001$), AMTS ($P = 0.041$) and accompaniment outdoors ($P = 0.033$) were significant co-variables for 30-d mortality. Furthermore, age ($P < 0.001$),

gender ($P = 0.011$), ASA grade ($P < 0.001$), AMTS ($P < 0.001$) and accompaniment outdoors ($P = 0.033$) all significantly influenced mortality at 120 d. ASA ($P < 0.001$) and season ($P = 0.014$) had significant effect on the odds of undergoing surgery in under 36 h.

CONCLUSION

Weekend admission was not associated with increased time-to-surgery or mortality in hip fracture patients. Demographic factors affect mortality in accordance with previous published reports.

Key words: Weekend; Hip; Fracture; Mortality; Season

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The weekend effect is gaining academic and political interest. It is important to consider departmental set ups that avoid potentially increased mortality in sick patients admitted on the weekend. Here we evaluate hip fracture patients admitted to a United Kingdom teaching hospital prior to the recent media and political interest, in a centre that had been commended for its care of hip fracture patients. There is no increased mortality in those admitted on a weekend - confirming that it is possible to negate a "weekend effect" with the appropriate infrastructure for hip fracture patients.

Mathews JA, Vindlacheruvu M, Khanduja V. Is there a weekend effect in hip fracture patients presenting to a United Kingdom teaching hospital? *World J Orthop* 2016; 7(10): 678-686 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/678.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.678>

INTRODUCTION

Hip fractures related to fragility account for a significant clinical and economic burden on the NHS, especially in an ageing population. There are an estimated 70000 such fractures annually in the United Kingdom, commanding a cost of almost £2 billion a year^[1]. These patients have a high prevalence of co-morbidities reflected by the high level of mortality associated with hip fractures - up to 10% of patients die within 30 d^[2]. In recent years there have been many steps taken to optimise the quality of care in this group of patients. This includes the distribution of the joint British Orthopaedic Association (BOA)-British Geriatric Society (BGS) "blue book"^[1], the setting up of the United Kingdom National Hip Fracture Database (NHFD)^[3], the government initiative of a best practice tariff (BPT)^[4], and recent publication of NICE guideline CG124^[5].

The literature has highlighted some concern over the management of patients admitted over weekends, which represent periods of time involving lower staffing levels and potential shortfalls in care^[6]. North American

and Australasian studies have found patients with certain medical and surgical diagnoses admitted over the weekend had higher risk-adjusted mortality than patients admitted on weekdays^[6-8]. This potential "weekend effect" may be exaggerated in teaching hospitals^[7]. In addition, a recent Dr. Foster report suggested that within the United Kingdom, "access to treatment over a weekend is a weak link in the management of hip fractures"^[9]. This observation must be addressed, as "early surgery" is associated with significantly reduced risk of mortality^[10], and thus any delays linked to timing of admission may have important consequences.

Patients admitted with hip fracture often have multiple co-morbidities and can present with concomitant medical pathologies such as ischaemic heart disease, electrolyte imbalances, renal impairment and sepsis. The effective management of these, medical optimisation and access to timely surgery are key factors in the effective treatment of hip fractures and prevention of further complications. Thus, the objective of our study was to examine the potential "weekend effect" on patients presenting with acute fragility hip fracture to a United Kingdom teaching hospital. Our aim was to compare patients admitted on weekdays vs weekends to elucidate any differences in: (1) Time-to-surgery (within 36 h, or not); (2) 30-d mortality; and (3) 120-d mortality.

Our null hypothesis was that there would be no difference in time to surgery or mortality between weekday and weekend groups. In addition, we planned to analyse the effect of 9 other variables on the above outcomes: Age; gender; American Society of Anesthesiologist (ASA) grade; abbreviated mental test score (AMTS); fracture type; type of accommodation admitted from; walking ability outdoors; need for accompaniment outdoors and season.

MATERIALS AND METHODS

Between 1st April 2009 and 30th September 2011, 883 patients were admitted to our hospital with primary fragility hip fracture. Hip fracture was defined as "a fracture occurring in the area between the edge of the femoral head and 5 cm below the lesser trochanter". All these patients had detailed records prospectively created on the NHFD. We excluded those whose records were incomplete to avoid unknown confounders (missing data included details on where the patient was admitted from, preoperative mobility and cognitive status and adequate follow up). This left us a study sample of 816 patients with 100% complete datasets, who were all included in our study. The NHFD is an internet-based audit tool that collates a variety of details on patients admitted with acute hip fracture, including patient characteristics, fracture type, operative details and times of admission to A&E, admission to orthopaedic ward and time of surgery. Accurate dates of death were attained from electronic hospital patient records. The resulting dataset was then used to extrapolate accurate values for time-to-surgery (hours) and 30- and 120-d mortality rates. Of the 816

Table 1 Baseline characteristics, grouped by time of week admitted

Explanatory variable	Classification	Time of week	
		Weekday	Weekend
Age, yr mean (SD)	46.4-100.9 ($P = 0.779$) ²	83.1 (8.4)	82.6 (9.3)
Gender	Male	169	65
	Female (Female %) ($P = 0.733$) ¹	412 (70.90%)	170 (72.30%)
ASA grade median (IQR)	1-5 ($P = 0.282$) ²	3 (1)	3 (1)
AMTS median (IQR)	0-10 ($P = 0.924$) ²	8 (5)	8 (5)
Fracture type	Intertrochanteric	217	92
	Intracapsular - displaced	287	99
	Intracapsular - undisplaced	48	31
	Subtrochanteric (% Intracapsular-displaced) ($P = 0.097$) ¹	29 (49.40%)	13 (42.10%)
Admitted from	Own home	417	191
	Other (% Own home) ($P = 1.00$) ¹	110 (81.10%)	44 (81.30%)
Ability to walk outdoors	Wheelchair/bedbound/electric buggy	173	65
	Never goes outdoors		
	Two aids	54	20
	One aids	154	60
Accompaniment outdoors	No aids (% Wheelchair, etc.) ($P = 0.780$) ¹	200 (29.80%)	90 (27.70%)
	Wheelchair/bedbound/electric buggy	88	31
	Never goes outdoors		
	Yes	193	86
Season	No (% Wheelchair, etc.) ($P = 0.604$) ¹	300 (15.10%)	118 (13.20%)
	Spring	133	61
	Summer	183	54
	Autumn	160	73
	Winter (% Winter) ($P = 0.108$) ¹	105 (18.10%)	47 (20.00%)
Time of week	Weekday	581	0
	Weekend	0	235

¹Fisher's Exact test; ²Mann-Whitney *U* test. SD: Standard deviation; IQR: Interquartile range.

patients, 20 did not have surgery and thus were excluded from the analysis for time-to-surgery ($n = 796$).

Definitions

Patients who were admitted to A and E from Monday 8:00 AM and Friday 5:59 PM were placed in the "weekday" group. Those admitted between Friday 6:00 PM and Monday 7:59 AM were categorised as the "weekend" group, in line with the trust out-of-hours rota.

Statistical analysis

Baseline characteristics between the two groups were compared using Fisher's exact test (for categorical covariates) or Mann - Whitney *U* test (for continuous covariates).

Logistic regression was carried out on 3 outcomes of interest (all binary outcomes), using 10 explanatory variables: (1) the proportion of patients receiving surgery in less than 36 h; (2) 30-d mortality; and (3) 120-d mortality.

The co-variables used were: day of admission (weekday

vs weekend); age; gender; ASA grade; AMTS; type of accommodation admitted from; type of fracture; ability to walk outdoors, need for accompaniment outdoors and season. Logistic regression models were fitted and the "Enter" method was used in the regression models to incorporate the time of week variable, as this was the main interest of the study; forward model selection was then applied to the remaining nine covariates in order to select the most parsimonious model. A P -value < 0.05 was considered as significant. The statistical methods of this study were reviewed by Rebecca Harvey of the Centre for Applied Medical Statistics, University of Cambridge.

RESULTS

A total of 796 patients were included for the final analysis. The average age of these patients was 83.0 ± 8.7 years, with a gender ratio of 2.5:1 (581 females; 235 males). During the study period there were 581 admissions during weekdays and 235 during weekend periods. Baseline characteristics of the two groups were not statistically

Table 2 Time-to-surgery and mortality and of patients admitted with hip fracture, grouped and compared by time of week

Outcome variable	Classification	Time of week	
		Weekday	Weekend
Time to surgery (n = 796)	< 36 h	334	138
	> 36 h	233	91
	(% < 36 h) <i>P</i> > 0.05	(58.90%)	(60.30%)
30-d mortality (n = 816)	No	548	224
	Yes	33	11
	(% Yes) <i>P</i> > 0.05	(5.70%)	(4.70%)
120-d mortality (n = 816)	No	497	207
	Yes	84	28
	(% Yes) <i>P</i> > 0.05	(14.50%)	(13.50%)

Table 3 Estimated model coefficients for the multivariate logistic regression model - time to surgery

Outcome 1	Time to surgery (< 36 h)	n = 796		
Variable	Level	OR	95%CI	P-value
ASA grade	1-5	0.68	0.54, 0.85	0.001
Season	Winter (reference)			0.014
	Spring	1.89	1.21, 2.94	0.005
	Summer	1.7	1.11, 2.61	0.014
	Autumn	1.9	1.23, 2.92	0.004
Time of week	Weekday (reference)			
	Weekend	1.01	0.73, 1.39	0.975

ASA: American Society of Anesthesiologist.

different in any of the measured fields (Table 1). The most common type of fracture seen during our study period was the intracapsular and displaced neck of femur fracture (n = 386; 47.9%). Most patients (n = 662; 70.9%) were living in their own home and around a third (n = 290; 35.6%) of patients walked outdoors without the use of aids prior to injury.

None of the outcome measures were significantly different between the weekday and the weekend groups (Figure 1 and Table 2).

Outcome 1 - Time-to-surgery < 36 h (Table 3)

There was statistically no difference in the odds of time-to-surgery being less than 36 h between weekend and weekday patients (P = 0.975). As ASA increases by one unit, the expected odds of having a time-to-surgery of less than 36 h are reduced by 32% (P = 0.001; 95%CI: 0.54, 0.85) (Figure 2). The season also has a significant effect on undergoing surgery within 36 h (P = 0.014). Patients who were admitted in spring, summer or autumn all have greater odds of having a time to surgery of less than 36 h compared to the patients admitted in winter.

Outcome 2 - 30-d mortality

There was statistically no difference in the odds of mortality within 30 d between hip fracture patients admitted during the weekdays vs weekends (P = 0.842) (Table 4). ASA was a strongly significant covariate in

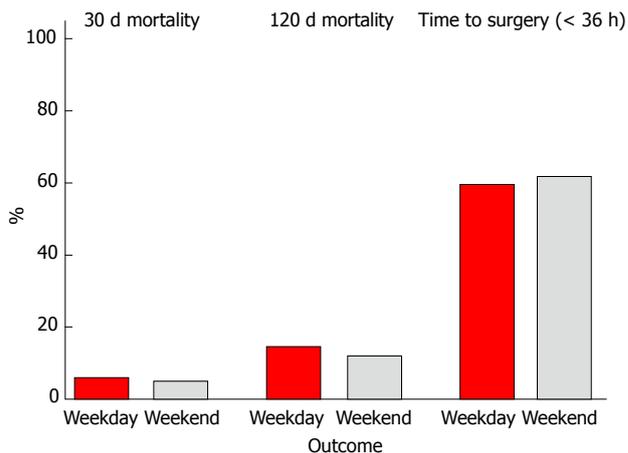


Figure 1 There was no significant difference in time-to-surgery < 36 h (P = 0.975) 30-d mortality (P = 0.842) or 120-d mortality (P = 0.425) between acute hip fracture patients admitted on weekdays (red bars) vs weekends (grey bars). All P-values derived from logistic regression model.

this model. As ASA grade increases by one unit, it is expected that the odds of dying by 30 d to be almost 2.7 times greater (P < 0.001) (Figure 2). Male patients had higher odds of mortality at 30 d than female patients [odds ratio (OR) 2.12; 95%CI: 1.09, 4.15] (Figure 3). It is expected that the 30-d mortality odds are lower as AMTS increases by one unit (P = 0.041); as AMTS increases by 1, the odds of dying at 30 d are reduced by 10% (95%CI: 0.81, 1.00) (Figure 4). Patients requiring accompaniment outdoors (P = 0.015) and those using a wheelchair or never go outdoors (P = 0.011) both have higher odds of mortality at 30 d compared with those who do not need any accompaniment outside (Figure 5). Wheelchair-bound patients have the greatest odds relative to those not requiring accompaniment outdoors - they are expected to have 5 times the odds of 30-d mortality. Other co-variables were not significant on this outcome.

Outcome 3 - 120-d mortality

There is no difference in odds of 120-d mortality between the weekend and the weekday groups (P-value = 0.425) (Table 4). As ASA increases by one unit, we would expect the odds of 120-d mortality to be 2 times greater (P < 0.001) (Figure 2). At 120 d, male patients have greater odds of dying but the expected increase in odds is lower than at 30 d. Male patients are expected to have 1.85 greater odds of mortality at 120 d (95%CI: 1.15, 2.98) (Figure 3). As AMTS increases by a unit, it would be expected that the odds of death at 120 d decrease by around 11% (P = 0.001) (Figure 4).

As age increases by one year, the odds of dying at 120 d are 1.06 times greater, i.e., an age increase of one year yields a 6% increase in 120-d mortality (95%CI: 1.03, 1.10). Patients who require a wheelchair to go outdoors or patients who don't go outside have more than twice the odds of 120-d mortality than patients who don't need accompaniment outdoors (P = 0.022) (Figure 5). There is however statistically no

Table 4 Estimated model coefficients for the multivariate logistic regression model - mortality

Outcome 2 30-d mortality		n = 816			Outcome 3 120-d mortality		n = 816		
Variable		OR	95%CI	P-value			OR	95%CI	P-value
Gender	Female (reference)				Female (reference)				
	Male	2.12	1.09, 4.15	0.028	Male		1.86	1.15, 2.99	0.011
ASA grade	1-5	2.68	1.55, 4.62	< 0.001	1-5		2.03	1.39, 2.95	< 0.001
AMTS	0-10	0.9	0.81, 1.00	0.041	0-10		0.89	0.83, 0.95	0.001
Age (yr)					46-101		1.06	1.03, 1.10	< 0.001
Accompanied outdoors	No (reference)			0.033	No (reference)				0.033
	Yes	4.22	1.32, 13.47	0.015	Yes		1.29	0.70, 2.36	0.423
Time of week	Wheelchair/bedbound/electric buggy/does not go out	5.14	1.46, 18.09	0.011	Wheelchair/bedbound/electric buggy/does not go out		2.22	1.12, 4.38	0.022
	Weekday (reference)				Weekday (reference)				
	Weekend	0.93	0.44, 1.94	0.842	weekend		0.82	0.50, 1.34	0.425

AMTS: Abbreviated Mental Test Score; ASA: American Society of Anesthesiologist.

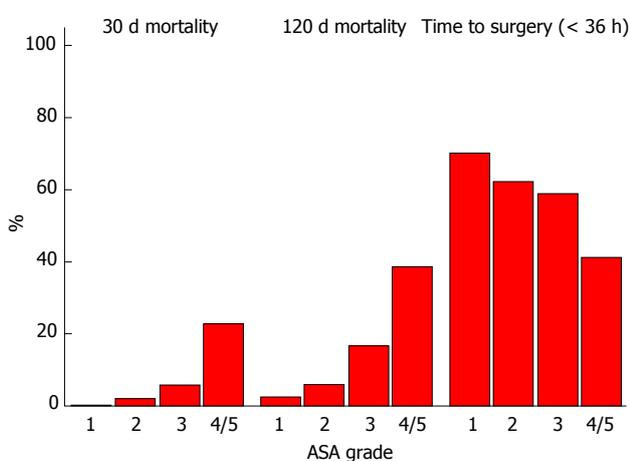


Figure 2 American Society of Anesthesiologist grade of patients admitted with hip fracture had a significant effect on 30-d mortality ($P < 0.001$), 120-d mortality ($P < 0.001$) and time to surgery ($P = 0.001$). As ASA increased, the mortality rate at 30- and 120-d increased, whilst the percentage of patients undergoing surgery within 36 h decreased. Percentages are expressed as means. All P -values derived from logistic regression model. ASA: American Society of Anesthesiologist.

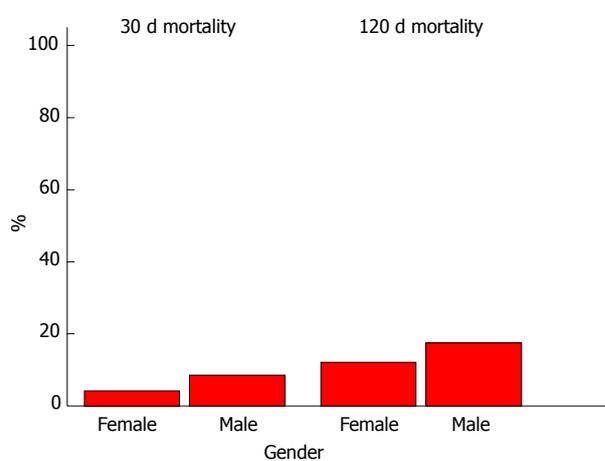


Figure 3 Gender of patients admitted with acute hip fracture had a significant influence on 30-d mortality ($P = 0.028$) and 120-d mortality ($P = 0.011$), with males having an increased risk of death at the two time cut-offs. Percentages are expressed as means. All P -values derived from logistic regression model.

difference in odds of dying between non wheelchair bound patients who need accompaniment outdoors and patients who do not require accompaniment outdoors. Other co-variates were not significant on this outcome

DISCUSSION

This study examines the potential weekend effect in patients with a hip fracture in a single teaching hospital within the United Kingdom; it reveals no statistical difference in either 30- or 120-d mortality between patients admitted to our tertiary referral hospital on weekdays vs weekends. In addition, patients admitted on the weekend were equally likely to undergo surgery within 36 h.

Hip fractures represent a common and serious injury in older people. Surgery is the main stay of treatment, with over 98% of patients undergoing operative fixation^[3]. The association of early surgery

with lower mortality rates in these patients has been widely published^[10]. Whilst national NICE guidelines recommend that surgery be performed “on the day of, or the day after admission”^[5], the government has introduced the “BPT”^[4]. The BPT offers hospitals a £1335 “bonus” payment per hip fracture patient that is managed according to a set of quality indicators, which include performing surgery within 36 h of admission, in combination with orthogeriatric led medical care in the acute phase and secondary fracture prevention. The BPT aims to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services. Accordingly, it has become a target for orthopaedic departments across the country to achieve surgery within the 36-h window and thus we chose that cut-off for this study.

Previous studies

Admissions over the weekend and other out-of-hour periods have been associated with undesirable

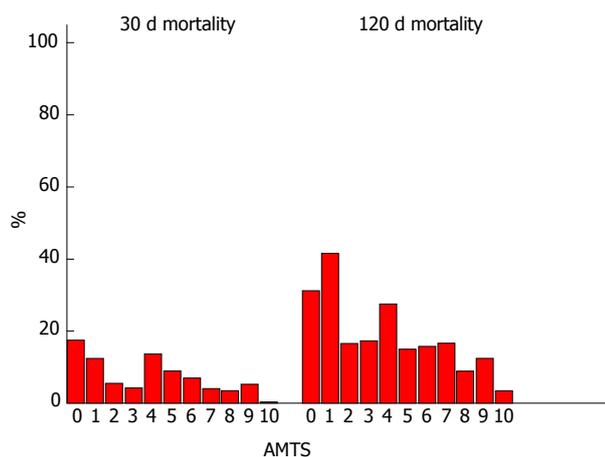


Figure 4 As Abbreviated Mental Test Score increased, 30-d mortality ($P = 0.041$) and 120-d mortality ($P = 0.001$) decreased in patients admitted with acute hip fracture. Percentages expressed as means. All P -values derived from logistic regression model. AMTS: Abbreviated Mental Test Score.

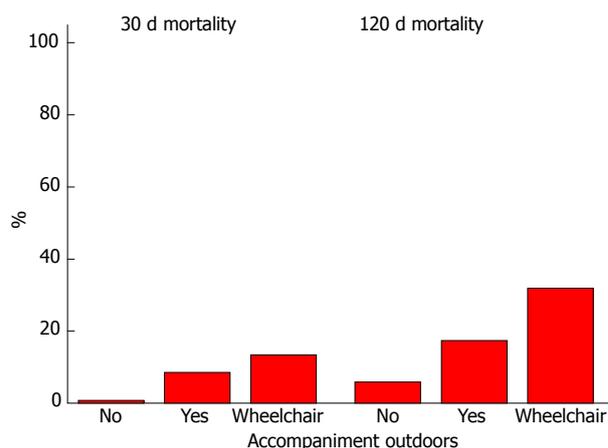


Figure 5 Requirement for accompaniment outside in hip fracture patients significantly influenced 30-d ($P = 0.033$) and 120-d mortality ($P = 0.033$). At 30 d, patients who are wheelchair bound, bedbound or do not go outside have a higher risk of death than those requiring no accompaniment outdoors, at 30 d and 120 d. In addition, patients requiring accompaniment outdoors have a higher at 30-d mortality than those who do not ($P = 0.015$), but this difference is abolished by 120 d ($P = 0.423$). Percentages are expressed as mean. All P -values derived from logistic regression model.

delays in investigations and procedures for certain conditions. A report recently published by the Agency for Healthcare Research and Quality (AHRQ) suggested that patients admitted over the weekend in the United States had significantly longer waits for various major procedures^[11]. The 2011 Dr. Foster report highlighted that there may be significant delays to hip fracture surgery associated with timing of admission in the United Kingdom, highlighting that many trusts are significantly worse at operating at the weekend^[9].

In addition, past research has shown that weekend admission is associated with increased mortality in certain diagnoses, attributing their findings to lower staffing levels and unreliable access to clinical services. Studies from Canada, United States and Australia have shown patients with ruptured abdominal aortic aneurysm (AAA)^[6], pulmonary embolism^[6], duodenal ulcers^[7] and ischaemic heart disease^[7,8] have a significantly increased risk of mortality if admitted during the weekend rather than weekday. More recently, evidence of a weekend effect for emergency conditions has also been reported in the United Kingdom^[12]. These studies did not observe an increase in mortality in hip fracture patients. However, a Danish study looking at 600 patients presenting with acute hip fracture, did find a significantly higher rate of mortality for those admitted over holiday periods^[13], another time group with limitations in human resources. One previous study has observed a potential weekend effect for hip fracture patients in a different United Kingdom teaching hospital^[14]. However, following reports of no weekend effect at national level in the United States^[15], it was clear that this may not be the case at other similar United Kingdom institutions and it is essential that this is shown.

Interpretation of results

Our data shows that being admitted with a hip fracture on the weekend has no negative impact on whether

patients undergo surgery within 36 h, at our centre. This is likely to be due to the fact this hospital runs a dedicated trauma list, with an allocated anaesthetist and on call theatre radiographer 7 d/wk. In centres where this is not available, the potential improvement in surgical delay with the addition of extra trauma theatre time has been emphasized^[16,17]. In addition we have a trauma nurse specialist heavily involved with the management of patients and organisation of trauma lists on every Saturday, in addition to weekdays. Despite these resources available, we found that around 16% of our cases are still delayed whilst awaiting trauma list space underlining the considerable room for further improvement^[3]. Indeed, only around 60% of patients achieve surgery within 36 h - however, this is a relatively new target that was introduced in April 2010, and the NHFD report shows this number to be improving nationwide since then^[3].

Our study also reveals an inverse relationship between the ASA grade and the time to surgery. This probably translates to patients with more co-morbidities requiring longer to undergo appropriate tests prior to transfer and achieve pre-operative optimization. Indeed, the NHFD report for 2010-2011 suggested that almost 1/3 of the fragility hip fracture patients in the United Kingdom who did not receive an operation within 36 h were delayed because they were awaiting medical review, investigation or stabilization^[3]. The number of patients falling into this group may be greater on weekends in some smaller United Kingdom centres where there are potentially only one or two general medical registrars on site; our centre is fortunate to have subspeciality medical registrars (*e.g.*, cardiology, respiratory) on call as well during the weekends. Thus speciality review and special investigations may have a greater probability of being achieved on admission,

which could reduce potential delays in optimisation for surgery.

Interestingly, we found that patients admitted during spring, summer or autumn were statistically more likely to go for surgery within 36 h than those who presented in winter. Higher fracture rates during winter have been reported for various types fracture in the United Kingdom, including hip fractures^[18,19]. It may be that patients admitted with hip fracture over winter are more likely to have an acute medical illness which has predisposed them to an increase risk of falls. Additionally, adverse weather conditions may have led to an increase in other non hip fractures, which may be reflected by longer time-to-surgery for patients in our study.

Our model did not find any significant difference in 30- or 120-d mortality between those admitted on weekends when compared with weekday admissions, supporting the null hypothesis. However, logistic regression of our data revealed that patients who were older, male, or had a higher ASA grade or lower AMTS at admission had a significantly higher risk of mortality, which correlates with previous observations^[20]. In addition, those who were wheelchair bound or did not go outside had a significantly increased odd of mortality, which may reflect the severity of co-morbidities in these patients. Baseline characteristics were not different between the two groups. Early surgery following hip fracture has been shown to significantly reduce morbidity and mortality when compared with delayed surgery^[13]. Thus, the fact there was no statistical difference between weekday and weekend groups in time-to-surgery within 36 h, nor mortality, suggests the outcomes are likely to be linked in our study. Whilst significant blood loss following hip fracture has been reported^[21], and such injuries may occur as a result of cardiorespiratory deterioration, it is not a diagnosis that is as susceptible to delays in definitive treatment as those mentioned above that do exhibit a weekend effect. These diagnoses, such as ruptured AAA, PE, and MI would be expected to have a much faster, more dramatic effect on haemodynamic stability.

Messages for clinicians and policy makers

Our data reveals that the overall 30-d mortality for patients presenting with hip fractures to our unit between April 2009-September 2011 was 5.4%. This is notably better than the widely reported figure of 10%^[3]; this lower rate has been previously acknowledged and commended^[22]. We have an established orthogeriatric service which directs peri- and post-operative medical optimisation of these patients. Regular medical input by such a team allows a continuity of care not afforded by previous systems where issues were dealt with by the on-call medical registrar of the day. In addition, our multidisciplinary rehabilitation team includes regular input from trauma nurse specialists, and 7 d/wk physiotherapy and occupational therapy service,

with emphasis placed on providing falls assessment and commencing bone protection medication during the admission. This highlights the potential positives of adhering to the indicators set out by the BPT^[4].

The aim of the BPT, which offers £1335 more than base tariff per case, is to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services. This should "stimulate better quality service provision which is more cost effective"^[4]. Our findings suggest that such funding would be well spent in developing additional trauma theatre time and further enhancing services over the weekend including physiotherapy, orthogeriatrics, trauma anaesthetists and theatre radiographers. Whilst guidelines encourage surgery to be performed during "normal working hours", there may be an argument to routinely extend the length of trauma lists to the twilight period to achieve better outcomes and aid qualification for the economic incentive described above.

Limitations

Our study does have limitations. The NHFD is an internet-based data collection system that was set up in 2007 following the long term success of databases such as the Scottish Hip fracture audit^[23]. It collates a wealth of information making it a powerful clinical audit tool, especially as data is collected prospectively. As with any database the information available is subject to error during data entry. Some fields such as were missing for certain patients resulting in exclusion of patients from our study. Importantly, baseline characteristics were not statistically different between weekday and weekend groups, either prior to or following exclusion though. The risk of future missing data has been minimised by appointment of an elderly trauma nurse specialist whose role includes ensuring accuracy, appropriateness and completeness of database entries.

We chose to maximise the number of patients we could analyse by including all patients who we could ascertain 120-d mortality data. In addition, it was necessary to amalgamate some groups to allow analysis, as individual groups (*e.g.*, those with ASA 4 or 5) would not have contained sufficient patients otherwise. Future studies should aim to explore if any difference exists in the longer term, for instance at 1 year, and should be of sufficient size to have adequate numbers in each category for analysis.

Future work

The management of hip fracture and resources available at different trusts vary considerably; it was the recognition of this fact which initiated the immense nationwide effort towards clinical governance outlined in this paper. Accordingly, it would be naïve to infer that the findings described at our tertiary referral centre hold true for all other hospitals in the United Kingdom. Previous studies have suggested that weekend effects

are amplified in teaching hospitals^[7]. This may not be the case in hip fracture surgery, if indeed there is a weekend effect to be found in other hospitals. The NHFD does however represent a useful instrument with which to analyse this potential weekend effect on a national basis, perhaps including a comparison between outcomes at teaching vs district general hospitals, as has previously been done in other countries^[7].

ACKNOWLEDGMENTS

We would like to give special thanks to Jane Hall, who helped collect the local data for the NHFD. We are also grateful to Rebecca Harvey for helping us with the data analysis and interpretation, using her expertise in medical statistics.

COMMENTS

Background

The weekend effect is gaining academic and political interest. Here we evaluate hip fracture patients admitted to a United Kingdom teaching hospital prior to the recent media and political interest, in a centre that had been commended for its care of hip fracture patients. Departments in the United Kingdom are encouraged to aim to medically optimise and operate on all hip fracture patients within 36 h if medically stable. However, hospitals around the country are very heterogeneous in their infrastructure. It is important to consider departmental set ups that avoid potentially increased mortality in sick patients admitted on the weekend.

Research frontiers

The weekend effect refers to the differential on mortality between patients admitted on a weekday with a given diagnosis, when compared with those admitted on a weekend with the same diagnosis. It is encouraged that hip fracture patients are operated on within 36 h of admission in the United Kingdom. This is financially incentivized as this time target is one of the criteria for the best practice tariff (BPT) (see terminology).

Innovations and breakthroughs

Whilst large population studies are incredibly useful at exploring the presence of weekend effect within a whole system, it is also important to check for its presence within heterogeneous departments within that overall system. This allows comparison and elucidation of potential targets to attenuate such differences. This study shows no weekend effect at this United Kingdom teaching hospital for hip fracture patients, in contrast with findings from other teaching hospitals. Increased orthogeriatrics involvement and 7 d/wk orthopaedic trauma lists are likely factors that negate the weekend effect.

Applications

Departments should explore the weekend effect in their departments to highlight areas for service improvement.

Terminology

BPT - the United Kingdom government has introduced the BPT. The BPT offers hospitals a £1335 "bonus" payment per hip fracture patient that is managed according to a set of quality indicators, which include performing surgery within 36 h of admission, in combination with orthogeriatric led medical care in the acute phase and secondary fracture prevention. The BPT aims to financially incentivise best clinical practice in hip fracture management and thus enable targeted investment back into local hip fracture services.

Peer-review

Authors compared mortality and time-to-surgery of patients admitted with hip fracture to their teaching hospital on weekdays vs weekends. As an

observational report, it is an interesting study of weekend effect on hip fracture patients. Experiments are generally well conducted and the manuscript is well written.

REFERENCES

- 1 The care of patients with a fragility fracture. Published by the British Orthopaedic Association, 2007. [accessed 2011 Nov 21]. Available from: URL: <http://www.fractures.com/pdf/BOA-BGS-Blue-Book.pdf>
- 2 Roche JJ, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ* 2005; **331**: 1374 [PMID: 16299013 DOI: 10.1136/bmj.38643.663843.55]
- 3 The National Hip Fracture Database National Report 2011. [accessed 2011 Dec 4]. Available from: URL: http://www.nhfd.co.uk/003/hipfractureR.nsf/NHFDNationalReport2011_Final.pdf
- 4 Best Practice Tariff for Hip Fracture- Making ends meet. British Geriatrics Society. [accessed 2011 Nov 28]. Available from: URL: http://www.bgs.org.uk/index.php?option=com_content&view=article&id=700:tariffhipfracture&catid=47:fallsandbones&Itemid=307
- 5 Hip fracture: the management of hip fracture in adults. NICE clinical guideline CG124; issued June 2011. [accessed 2011 Nov 27]. Available from: URL: <http://www.nice.org.uk/nicemedia/live/13489/54919/54919.pdf>
- 6 Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001; **345**: 663-668 [PMID: 11547721 DOI: 10.1056/NEJMsa003376]
- 7 Cram P, Hillis SL, Barnett M, Rosenthal GE. Effects of weekend admission and hospital teaching status on in-hospital mortality. *Am J Med* 2004; **117**: 151-157 [PMID: 15276592 DOI: 10.1016/j.amjmed.2004.02.035]
- 8 Clarke MS, Wills RA, Bowman RV, Zimmerman PV, Fong KM, Coory MD, Yang IA. Exploratory study of the 'weekend effect' for acute medical admissions to public hospitals in Queensland, Australia. *Intern Med J* 2010; **40**: 777-783 [PMID: 19811554]
- 9 Inside your hospital - Dr Foster Hospital Guide 2001-2011. [accessed 2011 Dec 7]. Available from: URL: http://drfosterintelligence.co.uk/wpcontent/uploads/2011/11/Hospital_Guide_2011.pdf
- 10 Simunovic N, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, Debeer J, Bhandari M. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ* 2010; **182**: 1609-1616 [PMID: 20837683 DOI: 10.1503/cmaj.092220]
- 11 Ryan K, Levit K, Hannah Davis PH. Characteristics of Weekday and Weekend Hospital Admissions. Rockville, MD, HCUP Statistical Brief #87. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006-2010 Mar [PMID: 21452494]
- 12 Freemantle N, Richardson M, Wood J, Ray D, Khosla S, Shahian D, Roche WR, Stephens I, Keogh B, Pagano D. Weekend hospitalization and additional risk of death: an analysis of inpatient data. *J R Soc Med* 2012; **105**: 74-84 [PMID: 22307037 DOI: 10.1258/jrsm.2012.120009]
- 13 Foss NB, Kehlet H. Short-term mortality in hip fracture patients admitted during weekends and holidays. *Br J Anaesth* 2006; **96**: 450-454 [PMID: 16443639 DOI: 10.1093/bja/ael012]
- 14 Thomas CJ, Smith RP, Uzoigwe CE, Braybrooke JR. The weekend effect: short-term mortality following admission with a hip fracture. *Bone Joint J* 2014; **96-B**: 373-378 [PMID: 24589794 DOI: 10.1302/0301-620X.96B3.33118]
- 15 Boylan MR, Rosenbaum J, Adler A, Naziri Q, Paulino CB. Hip Fracture and the Weekend Effect: Does Weekend Admission Affect Patient Outcomes? *Am J Orthop* (Belle Mead NJ) 2015; **44**: 458-464 [PMID: 26447407]
- 16 Marsland D, Chadwick C. Prospective study of surgical delay for hip fractures: impact of an orthogeriatrician and increased trauma capacity. *Int Orthop* 2010; **34**: 1277-1284 [PMID: 19838708 DOI:

- 10.1007/s00264-009-0868-0]
- 17 **Bhattacharyya T**, Vrahas MS, Morrison SM, Kim E, Wiklund RA, Smith RM, Rubash HE. The value of the dedicated orthopaedic trauma operating room. *J Trauma* 2006; **60**: 1336-1340 [PMID: 16766980 DOI: 10.1097/01.ta.0000220428.91423.78]
 - 18 **Crawford JR**, Parker MJ. Seasonal variation of proximal femoral fractures in the United Kingdom. *Injury* 2003; **34**: 223-225 [PMID: 12623255 DOI: 10.1016/S0020-1383(02)00211-5]
 - 19 **O'Neill TW**, Cooper C, Finn JD, Lunt M, Purdie D, Reid DM, Rowe R, Woolf AD, Wallace WA. Incidence of distal forearm fracture in British men and women. *Osteoporos Int* 2001; **12**: 555-558 [PMID: 11527052 DOI: 10.1007/s001980170076]
 - 20 **Gunasekera N**, Boulton C, Morris C, Moran C. Hip fracture audit: the Nottingham experience. *Osteoporos Int* 2010; **21**: S647-S653 [PMID: 21058005 DOI: 10.1007/s00198-010-1426-8]
 - 21 **Smith GH**, Tsang J, Molyneux SG, White TO. The hidden blood loss after hip fracture. *Injury* 2011; **42**: 133-135 [PMID: 20236640 DOI: 10.1016/j.injury.2010.02.015]
 - 22 Hospital Guide 2010: What makes a good hospital. [accessed 2011 Nov 28]. Available from: URL: <http://www.drfoosterhealth.co.uk/docs/ospital-guide-2010.pdf>
 - 23 Scottish Hip fracture Audit: Report 2008. Information and statistics division NHS services Scotland. [accessed 2012 Jan 12]. Available from: URL: <http://www.show.scot.nhs.uk/shfa>

P- Reviewer: Kuiper JWP, Maheshwari AV, Song GB **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Lu YJ



Randomized Controlled Trial

Volar locking distal radius plates show better short-term results than other treatment options: A prospective randomised controlled trial

Herwig Drobetz, Lidia Koval, Patrick Weninger, Ruth Luscombe, Paula Jeffries, Stefan Ehrendorfer, Clare Heal

Herwig Drobetz, Paula Jeffries, Orthopaedic Department, Mackay Base Hospital, James Cook University School of Medicine and Dentistry, Mackay, QLD 4740, Australia

Lidia Koval, Orthopaedic Department, the Prince Charles Hospital, Brisbane, QLD 4032, Australia

Patrick Weninger, Orthopaedic Hospital Speising, Vienna 1130, Austria

Ruth Luscombe, Mathematical Science School, Queensland University of Technology, Brisbane, QLD 4000, Australia

Stefan Ehrendorfer, Orthopaedic Department, Kantons Hospital Uri, 6460 Altdorf, Switzerland

Clare Heal, Department of General Practice, Mackay Base Hospital, James Cook University School of Medicine and Dentistry, Mackay, QLD 4740, Australia

Clare Heal, Anton Breinl Research Centre for Health Systems Strengthening, James Cook University, Townsville, QLD 4740, Australia

Author contributions: Drobetz H and Koval L designed this study; Koval L and Jeffries P collected data; Luscombe R conducted data analysis; all authors contributed to data analysis and interpretation; Heal C performed the statistical analysis and language editing; all authors drafted the manuscript and approved the final version.

Institutional review board statement: The study was approved by the Queensland Health ethics committee (approval number EC00407).

Clinical trial registration statement: The study was registered with Clinical Trials.gov (NCT00809861; DCDRS00407).

Informed consent statement: All study participants or their legal guardian, provided informed written consent prior to study enrolment.

Conflict-of-interest statement: There are no conflicts of interest declared.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Herwig Drobetz, MD, PhD, FAOrthA, FRACS, Orthopaedic Department, Mackay Base Hospital, James Cook University School of Medicine and Dentistry, Mackay Hospital and Health District, Bridge Road, Mackay, QLD 4740, Australia. herwig.dro@gmail.com
 Telephone: +61-7-48857900

Received: May 26, 2016

Peer-review started: May 27, 2016

First decision: July 6, 2016

Revised: July 27, 2016

Accepted: August 6, 2016

Article in press: August 8, 2016

Published online: October 18, 2016

Abstract

AIM

To compare the outcomes of displaced distal radius fractures treated with volar locking plates and with immediate postoperative mobilisation with the outcomes of these fractures treated with modalities that necessitate 6 wk wrist immobilisation.

METHODS

A prospective, randomised controlled single-centre trial

was conducted with 56 patients who had a displaced radius fracture were randomised to treatment either with a volar locking plate ($n = 29$), or another treatment modality ($n = 27$; cast immobilisation with or without wires or external fixator). Outcomes were measured at 12 wk. Functional outcome scores measured were the Patient-Rated Wrist Evaluation (PRWE) Score; Disabilities of the Arm, Shoulder and Hand and activities of daily living (ADLs). Clinical outcomes were wrist range of motion and grip strength. Radiographic parameters were volar inclination and ulnar variance.

RESULTS

Patients in the volar locking plate group had significantly better PRWE scores, ADL scores, grip strength and range of extension at three months compared with the control group. All radiological parameters were significantly better in the volar locking plate group at 3 mo.

CONCLUSION

The present study suggests that volar locking plates produced significantly better functional and clinical outcomes at 3 mo compared with other treatment modalities. Anatomical reduction was significantly more likely to be preserved in the plating group. Level of evidence: II.

Key words: Volar locking distal radius plate; Prospective randomised controlled; Postoperative mobilisation; Distal radius fracture; Short-term outcome

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The present study suggests that the treatment of distal radius fractures with volar locking distal radius plates and immediate postoperative mobilisation produces better functional, radiological and clinical outcomes at three months compared with other treatment modalities which necessitate six weeks immobilisation post fracture. Short term outcomes are very important in our view, as early mobility potentially means earlier return to activities of daily life and return to work for younger patients and remaining functionally independent for the elderly. Future studies should focus on cost savings gained by earlier return to activities of daily living.

Drobetz H, Koval L, Weninger P, Luscombe R, Jeffries P, Ehrendorfer S, Heal C. Volar locking distal radius plates show better short-term results than other treatment options: A prospective randomised controlled trial. *World J Orthop* 2016; 7(10): 687-694 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/687.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.687>

INTRODUCTION

Distal radius fractures are the most common type of fracture of the human skeleton, with about ten percent of

the population sustaining a fracture at some point in their life^[1-3]. Despite the lack of clear evidence, the treatment of distal radius fractures with volar locking distal radius plates (VLDRPs) has become increasingly popular in the last decade^[4-8]. The driving force behind the development of VLDRPs was dissatisfaction with the results of conventional treatment modalities. Volar locking plates are expensive^[9-11], but they are the only modality that allows distal radius fracture treatment without postoperative immobilisation. All other treatments necessitate between four and eight weeks of wrist immobilisation. Several studies show that these theoretical advantages of VLDRP seem to be equalized after twelve to 24 mo^[12-22]. The data on short-term benefits are still unclear, because patients treated with VLDRP still often have their wrists immobilised postoperatively, rather than being allowed to use as tolerated^[12-22]. There are only a few studies that specifically allow immediate postoperative mobilisation^[23,24], however they did not report on short-term outcomes. The aim of our study was to evaluate short-term results of distal radius fracture treatment with VLDRP and with immediate postoperative wrist mobilisation as tolerated compared to treatment modalities with six weeks immobilisation (closed reduction and casting; Kirschner (K-) wires and casting; external fixation).

MATERIALS AND METHODS

Study design

We carried out a randomised controlled single-centre trial involving patients presenting with distal radial fractures. The study was approved by the Queensland Health ethics committee (approval No. EC00407) and was registered with Clinical Trials.gov (NCT00809861; DCDRS00407).

Setting and participants

The study was conducted at a regional general hospital in Mackay, Queensland, Australia, between June 2009 and December 2013.

The study participants were recruited by two of the study authors (Herwig Drobetz and Lidia Koval). Consecutive patients presenting with distal radial fractures were invited to take part in the trial. The principle researcher was responsible for collecting data. Demographic information was collected for all patients, as well as clinical information regarding presence of osteoporosis, diabetes, or any other predetermined significant medical conditions. Fracture type was recorded. At the end of the recruitment period the principle and associate investigators re-examined hospital records to fill in any missing data.

Eligibility criteria

All patients over the age of 18 years presenting to the Emergency Department or Fracture clinic with a distal radial fracture were eligible to participate in the study. Patients who had bilateral wrist fractures, compound fractures, a concurrent ipsilateral upper limb injury, a past

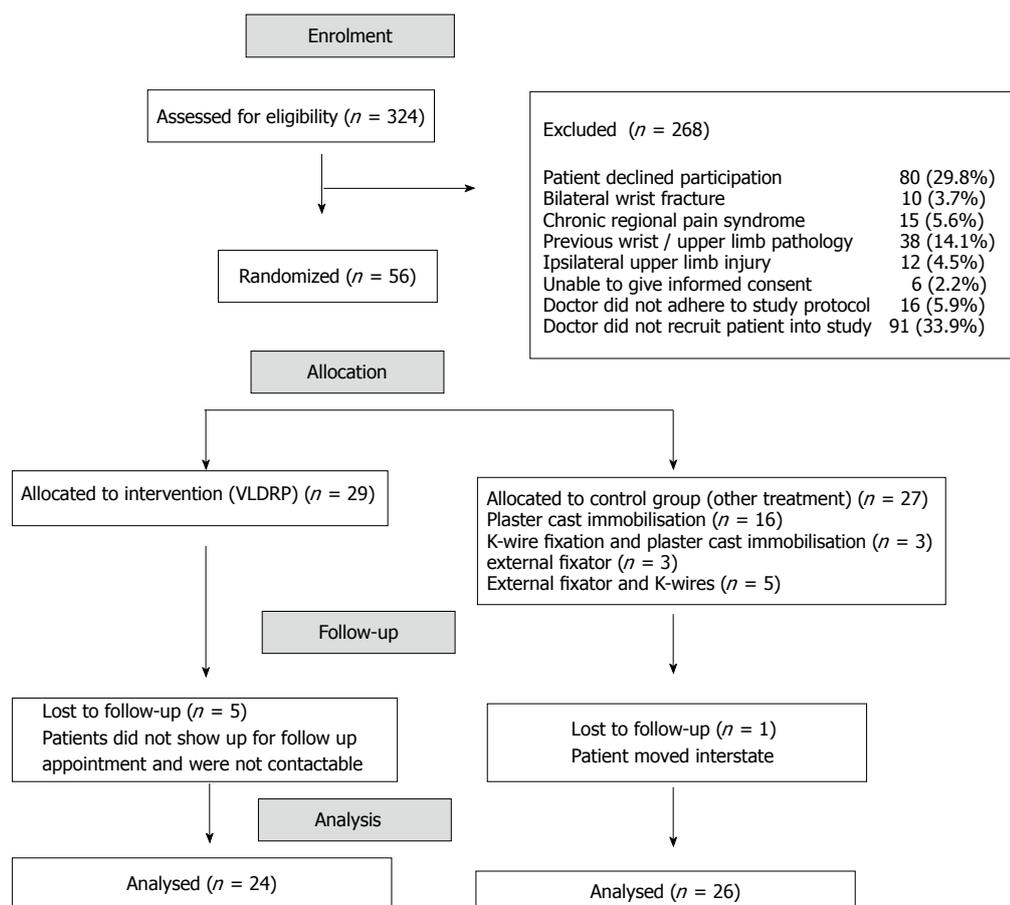


Figure 1 Consort flowchart of enrolment, exclusion, randomisation and follow up of patients. Patients were not recruited because they were overseas tourists or travelling or planning to move within the next twelve weeks.

history of chronic pain syndrome or history of pathology of ipsilateral extremity (including ipsilateral wrist) or who were unable to give informed consent were excluded from the study. Patients were also not included if the treating doctors concluded that they could not adhere to the study protocol (Figure 1).

Technique

All operations were performed by three consultant surgeons (including the principal investigator) at the Mackay Base Hospital Department of Orthopaedic surgery. The following technique was used.

Intervention (VLDRP): The fracture was approached using a volar Henry approach, reduced under fluoroscopic guidance and stabilised with a volar locking distal radius plate. All plates used were Synthes® (Synthes GmbH, Solothurn, Switzerland) VLDRPs, although different models (fixed and variable locking plates with either single or multiple distal screw holes). No bone graft or other void fillers were used. Postoperatively, patients were allowed to immediately use their wrist as tolerated without splinting or any other form of immobilisation. Patients were usually discharged from the hospital the day after the operation and were referred to a physiotherapist. The patients were seen at 2, 6 and 12

wk postoperatively.

Control group (non-operative, K-wire fixation and external fixator):

The patients in the control group received either: Closed reduction and casting ($n = 16$); closed reduction, K-wire fixation and casting ($n = 3$); or closed reduction and external fixation with ($n = 5$) or without ($n = 3$) additional K-wires (Figure 1). The same cohort of surgeons who performed the operations in the intervention group also treated the patients in the control group and were free to choose the control group treatment modality. All patients in the control group had their wrist immobilised for six weeks. K-wires and/or external fixators were removed at six weeks. The patients were seen weekly for cast checks/changes or pin checks. Patients were referred for physiotherapy after removal of the cast or external fixator. All patients were then seen again at 12 wk.

Recruitment and randomisation

All patients gave written informed consent before enrolling in the study. After agreeing to participate, patients were randomised using computer generated random numbers and opaque sealed envelopes. The principle investigator enrolled patients and assigned participants to their groups. All participating patients received written instructions on

post-operative care.

Outcomes

Follow up was conducted at 12 wk and comprised patient reported (functional), clinical and radiological outcomes. Only the principle investigator performed the assessments.

Functional assessment: Two self-administered standard questionnaires were given to the study participants [Disabilities of the Arm Shoulder and Hand (DASH) Outcome Measure^[25] and Patient Rated Wrist Evaluation (PRWE)]^[26] to measure disability at the three-month visit. Patients were assessed for their ability to perform activities of daily life (ADL) by being asked if they had resumed driving, and if employed if they had resumed working. They were further asked to grade their ability to perform ADLs into five categories (Group 1 = 100%; Group 2 = 75%-100%; Group 3 = 50%-75%; Group 4 = 25%-50%; Group 5 = 0%-25%). Not being able to drive or work at the 3 mo mark immediately precluded patients from classification into group 1 or 2. The measurement of ADLs was considered to be a secondary outcome measurement.

Clinical assessment: The range of movement of the wrist was assessed with use of a standard goniometer. Wrist strength was measured with use of a dynamometer (Jamar Hydraulic Hand Dynamometer; Lafayette Instrument[®], Lafayette, IN, United States). All clinical assessments were performed by the principle investigator (Herwig Drobetz) to reduce inter-observer variability.

Radiological assessment: Radiographs of the wrist taken pre-operatively, post reduction/postoperatively and at three months were assessed for study purposes. Volar tilt of the distal radius joint surface and anterior-posterior radial inclination were measured in degrees and ulnar variance as an indicator of radius shortening was measured in millimetres. Negative values for volar tilt represent dorsal tilt, and negative values for ulnar variance represent an ulna that is shorter than the radius. All radiological measurements were made by an independent assessor (Paula Jeffries) and validated by a radiologist. It was pre-determined that any inter-observer discrepancy of > 15% would trigger another review.

Sample size

Sample size was calculated on the basis of the validated DASH scale, in which a 20-point difference is considered to be clinically significant. Group sample sizes of 21 and 21 achieve 82% power to detect a difference of 20.0 between the null hypothesis assuming that both group means are 40.0 and the alternative hypothesis that the mean of group 2 is 20.0 with estimated group standard deviations of 20.0 and 20.0 and with a significance level (alpha) of 0.025 using a two-sided two-sample *t*-test. Therefore 21 patients were required in the intervention

and control groups. The sample size was set to a total of 46 patients to allow for drop out. The sample size calculation was based on the clinically significant difference for DASH in 2008 being considered to be 20.

Statistical analysis

All analysis was based on the intention-to-treat principal. Depending on the distribution, numerical data was described as mean value and SD or median value and inter-quartile range (IQR). Comparisons between intervention and control groups were conducted using bivariate statistical tests of the statistical programme SPSS (SPSS for Windows, version 22, SPSS Inc., Chicago, IL, United States). *P*-values less than 0.05 were considered to be statistically significant.

RESULTS

Of the total of 324 patients who presented with distal radial fractures during the study period from November 2009 to December 2013, 268 patients were excluded. Of the remaining 56 patients, 29 patients were randomised to the intervention (VLDRP) group, and 27 to the control (other treatments) group. A total of six patients were eventually lost to follow up because they failed to return for the 3-mo review. Follow up was completed in 50/56 (89%) randomised patients (Figure 1). Patients who completed the trial did not differ demographically, clinically or in terms of fracture severity from the group who were eligible for recruitment.

Comparisons at baseline

There were no significant differences between the intervention and the control groups at baseline (Table 1). Fracture types were comparable between groups.

Functional/clinical outcomes

The PRWE scores were significantly better in the VLDRP group than the control group at three months. The mean score in the VLDRP group was 21 compared to a mean score of 47 in the control group. This is also clinically significant as the minimum clinically important difference (MCID) is between 11 and 14 for the PRWE score^[27,28]. ADLs were significantly better at three months in the VLDRP group. Twenty patients were able to drive or work at 3 mo (group 1 or 2) in the VLDRP group compared with 15 patients in the control group (Table 2). The DASH scores were also better but this did not reach statistical significance. Wrist extension was significantly better in the VLDRP group as well as grip strength.

Radiological outcomes

At 3 mo, all radiological parameters were significantly better in the VLDRP group than in the control group (Table 3).

Complications

In the VLDRP group we observed five complications in five patients at the three month follow up visit:

Table 1 Baseline comparisons of intervention (volar locking distal radius plate) and control (other treatments) group

	Intervention group <i>n</i> = 24	Control group <i>n</i> = 26
Patient characteristics		
Mean age (SD)	51.1 (16.0)	52.5 (16.5)
Gender F (M)	15 (9)	13 (13)
% Osteoporosis	43	47
% Diabetes mellitus	5	4
% With medical condition ¹	25	29
Dominant hand	9	12
Fracture classification		
A2	0	2
A3	4	7
B2	3	3
C1	7	6
C2	8	7
C3	2	1

¹Medical conditions recorded were COPD (3), Patient on aspirin or clopidogrel (5); oral steroids (1); continuous inhaled steroids (2); ischaemic heart disease (2). F: Female; M: Male.

Table 2 Functional and clinical outcomes at 3 mo

	VLDRP group <i>n</i> = 24	Control group <i>n</i> = 26	<i>P</i> -value
DASH (points)	40 (12)	50 (24)	0.063
PRWE (points)	21 (20)	47 (40)	0.007 ¹
Grip strength (% of grip strength of uninjured limb)	64 (29)	42 (32)	0.012 ¹
Range of motion (in degrees)			
Flexion	60 (21)	49 (22)	0.072
Extension	65 (48)	48 (27)	0.021 ¹
Pronation	70 (31)	68 (26)	0.805
Supination	82 (25)	79 (24)	0.677
ADLs			
Grade 1	19	10	0.036 ¹
Grade 2	1	5	
Grade 3	4	7	
Grade 4	0	2	
Grade 5	0	2	

The values are given as the mean and (standard deviation). ¹Indicates significant result. The DASH is a validated, self-reported thirty item metric of upper-extremity function based on a 100 point scale, with 0 points indicating no disability and 100 points indicating maximum disability. The PRWE is a 15-item questionnaire designed to measure wrist pain and disability in activities of daily living. The PRWE allows patients to rate pain and disability from 0 to 10, with 10 being worst pain/unable to perform an activity. ADL: Activities of daily life; VLDRP: Volar locking distal radius plate; DASH: Disabilities of the Arm Shoulder and Hand; PRWE: Patient-Rated Wrist Evaluation.

Flexor tendon rupture, *n* = 1 (patient refused tendon reconstruction); carpal tunnel syndrome, *n* = 1 (patient underwent nerve release after 6 mo); Chronic Regional Pain Syndrome (CRPS), *n* = 1. Two patients did not like “having a plate inside my body” and the plates were subsequently removed 4 mo postoperatively. There were no intra-operative or immediate postoperative complications.

In the control group we observed seven complications

Table 3 Radiological parameters at presentation, post reduction, and 3 mo follow-up

	VLDRP group <i>n</i> = 24	Control group <i>n</i> = 26	<i>P</i> -value
Injured wrist at presentation			
Volar slope (degrees)	-17.2 (17.2)	-13.4(14.4)	0.241
Radial inclination (degrees)	8.7 (7.6)	14.2 (9.4)	0.02 ¹
Ulnar variance (mm)	2.5 (2.2)	2.3 (3.3)	0.285
Injured wrist post-reduction			
Volar slope (degrees)	4.7 (5.4)	0.08(7.25)	0.01 ¹
Radial inclination (degrees)	19.6 (4.5)	18.69(4.52)	0.45
Ulnar variance (mm)	0.1 (0.6)	0.4 (1.4)	0.146
Injured wrist 3 mo			
Volar slope (degrees)	3.5 (4.6)	-5.4 (11.6)	0.001 ¹
Radial inclination (degrees)	19.3 (4.4)	15.37 (7.0)	0.054 ¹
Ulnar variance (mm)	0.9 (1.3)	2.1 (1.9)	0.011 ¹

The values are given as the mean and (standard deviation). ¹Indicates significant result. VLDRP: Volar locking distal radius plate.

in seven patients: Malunion, *n* = 2 (1 of which subsequently had a corrective osteotomy due to functional deficits); CRPS, *n* = 2; infected K-wires which had to be removed early, *n* = 3.

DISCUSSION

The results of our study suggest that clinical and radiological outcomes are superior in the VLDRP group when compared to treatment modalities that necessitate six weeks of wrist immobilisation at the 3-mo mark.

Currently there are no clear evidence based guidelines for the best treatment of distal radius fractures^[28]. There have been many encouraging results with the use of VLDRPs^[29-34] but other authors reported similar favourable results with other treatment modalities^[13,16,21,22,35].

As mentioned in the introduction, many studies show that after one to two years the results of all treatment modalities are similar and there are no longer any significant differences. This fact is often used as an argument against the use of VLDRPs. We do not agree, as the short-term outcomes of treatments are important for patient quality of life and morbidity. Getting back to work 6 wk earlier or, for elderly patients, staying independent can make a significant difference. This might also have an economical impact, as the Medicare savings with earlier return to ADLs can potentially offset the costs for the more expensive treatment with VLDRPs.

Furthermore, it holds true for almost every fracture we treat that long-term outcomes are similar regardless of the treatment, but short-term outcomes are favourable for the more invasive treatment modalities. Tibial shaft fractures treated with intramedullary nails show excellent functional short-term results. After 12 to 24 mo, however, the results are not significantly different from treatment of these fractures with cast immobilisation or an external fixator, both of which are significantly cheaper options^[36]. However, due to increased patient demands, the ability

to mobilise early and the fact that the overall short-term benefits are significantly greater, intramedullary nailing of tibial shaft fractures has become the gold-standard treatment.

There are several limitations to our study. Various factors influence the outcomes of distal radius fractures and although information on as many variables as possible was recorded, it proved difficult to ensure that baseline data was comparable. For example, the prevalence of osteopenia or osteoporosis was not verified by a computer tomography or bone densitometry but we used information from the patient's history or GP. Surgical training and technique of the surgeons involved is a potential confounder, which would be difficult to quantify and was not recorded. The study was not blinded, as the nature of surgical procedures, and related postoperative care cannot realistically be masked to patients and staff, and resulting scars preclude the blinding of a blinded independent outcome assessor.

DASH and PRWE, although validated questionnaires, are still subjective scores and especially the DASH has a lower specificity in reporting wrist problems^[37,38]. The clinical measurements may be subject to inter and intra-observer variation, although one clinician completed all measurements to reduce inter-observer error. Radiological measurements may also be subject to intra and inter-observer error. Two observers including a radiologist checked all radiographs to reduce errors.

We asked the study participants to subjectively rate their ability to perform specific ADLs with their injured wrist, compare them to their uninjured wrist and then quantify them. We are aware that this is not a validated score but to our knowledge there is no validated wrist specific ADL score available yet^[39]. The number of patients reporting full return to ADLs after twelve weeks in the VLDRP was, however, significantly higher than in the control group.

Another limitation is that the study had three different treatment types in the control arm. However, we felt it was unethical to use a single treatment modality as the control group for the purposes of the study, and we feel that this heterogeneous control group represents the "real-life" situation. Our main outcome measure was to see the effect of six weeks immobilization vs immediate mobilization.

There are some important strengths of this study. To our knowledge this is the first study that looked at immediate mobilisation vs immobilisation for the treatment of distal radius fractures. The study showed that distal radius fractures treated with VLDRP can be treated with immediate postoperative mobilisation without secondary loss of reduction. In a setting like Northern Queensland, where many patients live up to 600 km away from the hospital this constitutes an important factor as the number of follow up visits can potentially be significantly reduced. Treatment with plaster cast or external fixator necessitates more follow up visits and is generally more involved. While recent

European studies^[10,11] show significant cost savings with the use of K-wires over volar locking plates, this might be different in a regional Australian setting.

In conclusion, the evidence for using VLDRPs for the treatment of distal radius fractures is still a matter of debate and in addition to efficacy; costs and adverse effects should be taken into account. However, our study showed that in the short-term, the functional, clinical and radiological outcomes were superior in the VLDRP group in comparison to other treatment methods. We strongly believe we should concentrate on the early outcomes of distal radius fracture treatment with VLDRPs and not resign ourselves to the fact that "after time, they are all the same". Therefore, the results of this study could encourage the judicial use of VLDRPs for the treatment of distal radius fractures. Future studies should focus on cost savings gained by earlier return to ADLs.

COMMENTS

Background

Despite the lack of clear evidence, the treatment of distal radius fractures with volar locking distal radius plates (VLDRPs) has become increasingly popular in the last decade VLDRPs are the only treatment which allows distal radius fracture fixation without the need for postoperative immobilisation. Several studies show that advantages of VLDRP seem to be equalized after 12 to 24 mo, but there are little data available on short-term benefits of VLDRPs when combined with early mobilisation.

Research frontiers

The treatment of distal radius fractures with VLDRPs has been an area of increased research interest in the last ten years. Recently, many authors have focused on the fact that outcomes when compared with non-operative treatment are similar after 12 to 24 mo. There have also been recent publications showing that volar plating is significantly more expensive when compared to other treatment modalities. There are, however only very limited data on return to work and function in the short term. Earlier return of function and ability to work, which is potentially possible with volar locking plates could mean significant overall cost savings when compared to other treatment options which necessitate 6 wk of immobilisation.

Innovations and breakthroughs

The study showed that VLDRP produced significantly better functional and clinical outcomes at 3 mo compared with other treatment modalities. The study also showed that VLDRP patients can perform activities of daily life significantly earlier than patients who need 6 wk of wrist immobilisation. The study is the only study to the knowledge which allowed immediate postoperative wrist mobilisation after plating with VLDRPs. This allows accurate determination of early functional results, which in our opinion are crucial. All other studies the authors looked at immobilised the wrist for 2 to 4 wk postoperatively.

Applications

Short term benefits are very important, as they translate into the ability for patients to return to work earlier, improve patient quality of life and might have overall cost savings when patients can return to work potentially 6 wk earlier than patients treated with casts or external fixators.

Terminology

VLDRPs have been in clinical use since 1997. The difference to traditional plates is that the screws are connected to the plate in an angle stable fashion, mostly by a thread in the plate hole and in the screw head. This effectively creates a rake like construct. The stiffness of the construct and its ability to withstand deforming forces are therefore not dependant of the bone quality

anymore, as opposed to traditional plates, which need friction between bone and plate to create sufficient construct stiffness. This allows treatment of fractures from the "biomechanically wrong" volar side of the wrist - easier approach and better soft tissue coverage of the implants. It also allows immediate postoperative mobilisation of the wrist, a unique feature of VLDRPs.

Peer-review

It is a random controlled study involving patients presenting with distal radial fractures. Based on better functional, clinical and radiological outcomes at short-term follow-up, the authors encourage the use of volar locking plates for the treatment of distal radius fractures. The study is well designed and the data is reliable.

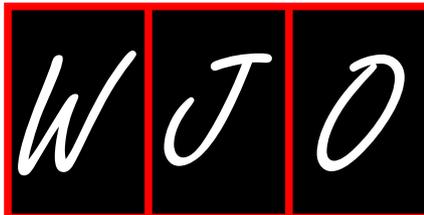
REFERENCES

- Graff S, Jupiter J. Fracture of the distal radius: classification of treatment and indications for external fixation. *Injury* 1994; **25** Suppl 4: S-D14-S-D25 [PMID: 7868191]
- Jupiter JB. Fractures of the distal end of the radius. *J Bone Joint Surg Am* 1991; **73**: 461-469 [PMID: 2002085]
- Tscherne H, Jähne J. [Current status of the treatment of distal radius fracture]. *Unfallchirurg* 1990; **93**: 157-164 [PMID: 2189226]
- Chung KC, Shauver MJ, Birkmeyer JD. Trends in the United States in the treatment of distal radial fractures in the elderly. *J Bone Joint Surg Am* 2009; **91**: 1868-1873 [PMID: 19651943 DOI: 10.2106/JBJS.H.01297]
- Mattila VM, Huttunen TT, Sillanpää P, Niemi S, Pihlajamäki H, Kannus P. Significant change in the surgical treatment of distal radius fractures: a nationwide study between 1998 and 2008 in Finland. *J Trauma* 2011; **71**: 939-942; discussion 942-943 [PMID: 21986738 DOI: 10.1097/TA.0b013e3182231af9]
- Chen NC, Jupiter JB. Management of distal radial fractures. *J Bone Joint Surg Am* 2007; **89**: 2051-2062 [PMID: 17768207 DOI: 10.2106/JBJS.G.00020]
- Tarallo L, Mugnai R, Zambianchi F, Adani R, Catani F. Volar plate fixation for the treatment of distal radius fractures: analysis of adverse events. *J Orthop Trauma* 2013; **27**: 740-745 [PMID: 23515129 DOI: 10.1097/BOT.0b013e3182913fc5]
- Mellstrand-Navarro C, Pettersson HJ, Tornqvist H, Ponzer S. The operative treatment of fractures of the distal radius is increasing: results from a nationwide Swedish study. *Bone Joint J* 2014; **96-B**: 963-969 [PMID: 24986952 DOI: 10.1302/0301-620X.96B7.33149]
- Dzaja I, MacDermid JC, Roth J, Grewal R. Functional outcomes and cost estimation for extra-articular and simple intra-articular distal radius fractures treated with open reduction and internal fixation versus closed reduction and percutaneous Kirschner wire fixation. *Can J Surg* 2013; **56**: 378-384 [PMID: 24284144 DOI: 10.1503/cjs.22712]
- Karantana A, Scammell BE, Davis TR, Whynes DK. Cost-effectiveness of volar locking plate versus percutaneous fixation for distal radial fractures: Economic evaluation alongside a randomised clinical trial. *Bone Joint J* 2015; **97-B**: 1264-1270 [PMID: 26330595 DOI: 10.1302/0301-620X.97B9.35560]
- Tubeuf S, Yu G, Achten J, Parsons NR, Rangan A, Lamb SE, Costa ML. Cost effectiveness of treatment with percutaneous Kirschner wires versus volar locking plate for adult patients with a dorsally displaced fracture of the distal radius: analysis from the DRAFFT trial. *Bone Joint J* 2015; **97-B**: 1082-1089 [PMID: 26224825 DOI: 10.1302/0301-620X.97B8.35234]
- Wilcke MK, Abbaszadegan H, Adolphson PY. Wrist function recovers more rapidly after volar locked plating than after external fixation but the outcomes are similar after 1 year. *Acta Orthop* 2011; **82**: 76-81 [PMID: 21281262 DOI: 10.3109/17453674.2011.552781]
- Wei DH, Raizman NM, Bottino CJ, Jobin CM, Strauch RJ, Rosenwasser MP. Unstable distal radial fractures treated with external fixation, a radial column plate, or a volar plate. A prospective randomized trial. *J Bone Joint Surg Am* 2009; **91**: 1568-1577 [PMID: 19571078 DOI: 10.2106/JBJS.H.00722]
- Egol K, Walsh M, Tejwani N, McLaurin T, Wynn C, Paksima N. Bridging external fixation and supplementary Kirschner-wire fixation versus volar locked plating for unstable fractures of the distal radius: a randomised, prospective trial. *J Bone Joint Surg Br* 2008; **90**: 1214-1221 [PMID: 18757963 DOI: 10.1302/0301-620X.90B9.20521]
- Wright TW, Horodyski M, Smith DW. Functional outcome of unstable distal radius fractures: ORIF with a volar fixed-angle tine plate versus external fixation. *J Hand Surg Am* 2005; **30**: 289-299 [PMID: 15781351 DOI: 10.1016/j.jhbsa.2004.11.014]
- Rozental TD, Blazar PE, Franko OI, Chacko AT, Earp BE, Day CS. Functional outcomes for unstable distal radial fractures treated with open reduction and internal fixation or closed reduction and percutaneous fixation. A prospective randomized trial. *J Bone Joint Surg Am* 2009; **91**: 1837-1846 [PMID: 19651939 DOI: 10.2106/JBJS.H.01478]
- Koshimune M, Kamano M, Takamatsu K, Ohashi H. A randomized comparison of locking and non-locking palmar plating for unstable Colles' fractures in the elderly. *J Hand Surg Br* 2005; **30**: 499-503 [PMID: 16061315 DOI: 10.1016/j.jhbs.2005.04.018]
- Chung KC, Squitieri L, Kim HM. Comparative outcomes study using the volar locking plating system for distal radius fractures in both young adults and adults older than 60 years. *J Hand Surg Am* 2008; **33**: 809-819 [PMID: 18656749 DOI: 10.1016/j.jhbsa.2008.02.016]
- Chung KC, Watt AJ, Kotsis SV, Margaliot Z, Haase SC, Kim HM. Treatment of unstable distal radial fractures with the volar locking plating system. *J Bone Joint Surg Am* 2006; **88**: 2687-2694 [PMID: 17142419 DOI: 10.2106/JBJS.E.01298]
- Karantana A, Davis TR. Extra-articular fractures of the distal radius--a European view point. *Hand Clin* 2012; **28**: 145-150 [PMID: 22554657 DOI: 10.1016/j.hcl.2012.03.001]
- Costa ML, Achten J, Parsons NR, Rangan A, Griffin D, Tubeuf S, Lamb SE. Percutaneous fixation with Kirschner wires versus volar locking plate fixation in adults with dorsally displaced fracture of distal radius: randomised controlled trial. *BMJ* 2014; **349**: g4807 [PMID: 25096595 DOI: 10.1136/bmj.g4807]
- Karantana A, Downing ND, Forward DP, Hatton M, Taylor AM, Scammell BE, Moran CG, Davis TR. Surgical treatment of distal radial fractures with a volar locking plate versus conventional percutaneous methods: a randomized controlled trial. *J Bone Joint Surg Am* 2013; **95**: 1737-1744 [PMID: 24088965 DOI: 10.2106/JBJS.L.00232]
- Shetty MS, Kumar MA, Kiran K, Kini AR. Locking distal radius plate--early results from India. *J Trauma* 2011; **71**: 1359-1363 [PMID: 21460739 DOI: 10.1097/TA.0b013e3182127c57]
- Osada D, Kamei S, Masuzaki K, Takai M, Kameda M, Tamai K. Prospective study of distal radius fractures treated with a volar locking plate system. *J Hand Surg Am* 2008; **33**: 691-700 [PMID: 18590852 DOI: 10.1016/j.jhbsa.2008.01.024]
- Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG) *Am J Ind Med* 1996; **29**: 602-608 [PMID: 8773720 DOI: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4>3.0.CO;2-L]
- MacDermid JC, Turgeon T, Richards RS, Beadle M, Roth JH. Patient rating of wrist pain and disability: a reliable and valid measurement tool. *J Orthop Trauma* 1998; **12**: 577-586 [PMID: 9840793 DOI: 10.1097/00005131-199811000-00009]
- Walenkamp MM, de Muinck Keizer RJ, Goslings JC, Vos LM, Rosenwasser MP, Schep NW. The Minimum Clinically Important Difference of the Patient-rated Wrist Evaluation Score for Patients With Distal Radius Fractures. *Clin Orthop Relat Res* 2015; **473**: 3235-3241 [PMID: 26040969 DOI: 10.1007/s11999-015-4376-9]
- Sorensen AA, Howard D, Tan WH, Ketchersid J, Calfee RP. Minimal clinically important differences of 3 patient-rated outcomes instruments. *J Hand Surg Am* 2013; **38**: 641-649 [PMID: 23481405 DOI: 10.1016/j.jhbsa.2012.12.032]

- 29 **Lichtman DM**, Bindra RR, Boyer MI, Putnam MD, Ring D, Slutsky DJ, Taras JS, Watters WC, Goldberg MJ, Keith M, Turkelson CM, Wies JL, Haralson RH, Boyer KM, Hitchcock K, Raymond L. Treatment of distal radius fractures. *J Am Acad Orthop Surg* 2010; **18**: 180-189 [PMID: 20190108 DOI: 10.5435/00124635-201003000-00007]
- 30 **Matschke S**, Marent-Huber M, Audigé L, Wentzensen A. The surgical treatment of unstable distal radius fractures by angle stable implants: a multicenter prospective study. *J Orthop Trauma* 2011; **25**: 312-317 [PMID: 21464738 DOI: 10.1097/BOT.0b013e3181f2b09e]
- 31 **Lattmann T**, Meier C, Dietrich M, Forberger J, Platz A. Results of volar locking plate osteosynthesis for distal radial fractures. *J Trauma* 2011; **70**: 1510-1518 [PMID: 21057334 DOI: 10.1097/TA.0b013e3181f13c6a]
- 32 **Jupiter JB**, Marent-Huber M. Operative management of distal radial fractures with 2.4-millimeter locking plates. A multicenter prospective case series. *J Bone Joint Surg Am* 2009; **91**: 55-65 [PMID: 19122079 DOI: 10.2106/JBJS.G.01498]
- 33 **Arora R**, Lutz M, Fritz D, Zimmermann R, Oberladstätter J, Gabl M. Palmar locking plate for treatment of unstable dorsal dislocated distal radius fractures. *Arch Orthop Trauma Surg* 2005; **125**: 399-404 [PMID: 15891921 DOI: 10.1007/s00402-005-0820-8]
- 34 **Orbay JL**, Fernandez DL. Volar fixed-angle plate fixation for unstable distal radius fractures in the elderly patient. *J Hand Surg Am* 2004; **29**: 96-102 [PMID: 14751111 DOI: 10.1016/j.jhssa.2003.09.015]
- 35 **Hull P**, Baraza N, Gohil M, Whalley H, Mauffrey C, Brewster M, Costa ML. Volar locking plates versus K-wire fixation of dorsally displaced distal radius fractures--a functional outcome study. *J Trauma* 2011; **70**: E125-E128 [PMID: 20693924 DOI: 10.1097/TA.0b013e3181e32714]
- 36 **Sarmiento A**. A functional below-the-knee brace for tibial fractures: a report on its use in one hundred and thirty-five cases. 1970. *J Bone Joint Surg Am* 2007; **89** Suppl 2 Pt.2: 157-169 [PMID: 17768212 DOI: 10.2106/JBJS.G.00188]
- 37 **Changulani M**, Okonkwo U, Keswani T, Kalairajah Y. Outcome evaluation measures for wrist and hand: which one to choose? *Int Orthop* 2008; **32**: 1-6 [PMID: 17534619 DOI: 10.1007/s00264-007-0368-z]
- 38 **Mellstrand Navarro C**, Ponzer S, Törnkvist H, Ahrengart L, Bergström G. Measuring outcome after wrist injury: translation and validation of the Swedish version of the patient-rated wrist evaluation (PRWE-Swe). *BMC Musculoskelet Disord* 2011; **12**: 171 [PMID: 21781287 DOI: 10.1186/1471-2474-12-171]
- 39 **Goldhahn J**, Beaton D, Ladd A, Macdermid J, Hoang-Kim A. Recommendation for measuring clinical outcome in distal radius fractures: a core set of domains for standardized reporting in clinical practice and research. *Arch Orthop Trauma Surg* 2014; **134**: 197-205 [PMID: 23728832 DOI: 10.1007/s00402-013-1767-9]

P- Reviewer: Ma DY, von Heideken J **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Lu YJ





Laminar screw fixation in the subaxial cervical spine: A report on three cases

Hironori Tanabe, Yoichi Aota, Tomoyuki Saito

Hironori Tanabe, Tomoyuki Saito, Department of Orthopedic Surgery, Yokohama City University, Yokohama 236-0004, Japan

Yoichi Aota, Department of Orthopedic Surgery, Yokohama Stroke and Brain Center, Yokohama 235-0012, Japan

Author contributions: Tanabe H performed acquisition of data, analyses and interpretation of data and drafted the manuscript; Aota Y conceptualized and designed the study and also critical revised the manuscript; Saito T approved the final version for the manuscript.

Institutional review board statement: This study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This study has received approval from the authors' institute review board.

Informed consent statement: Written informed consent was obtained from all patients.

Conflict-of-interest statement: The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Hironori Tanabe, MD, Department of Orthopedic Surgery, Yokohama City University, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan. iamhiro1978@yahoo.co.jp
Telephone: +81-45-7872655
Fax: +81-45-7817922

Received: February 27, 2016
Peer-review started: February 28, 2016

First decision: June 12, 2016

Revised: June 25, 2016

Accepted: August 15, 2016

Article in press: August 16, 2016

Published online: October 18, 2016

Abstract

Although laminar screw fixation is often used at the C2 and C7 levels, only few previous case reports have presented the use of laminar screws at the C3-C6 levels. Here, we report a novel fixation method involving the use of practical laminar screws in the subaxial spine. We used laminar screws in the subaxial cervical spine in two cases to prevent vertebral artery injury and in one case to minimize exposure of the lamina. This laminar screw technique was successful in all three cases with adequate spinal rigidity, which was achieved without complications. The use of laminar screws in the subaxial cervical spine is a useful option for posterior fusion of the cervical spine.

Key words: Laminar screw; Instrumentation; Subaxial cervical spine

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Laminar screw fixation is often used at the C2 and C7 levels, however, only few previous case reports have presented the use of laminar screws at the C3-C6 levels. In this article, the authors describe a novel fixation method involving the use of laminar screws in the subaxial spine with adequate spinal rigidity, which was achieved without complications.

Tanabe H, Aota Y, Saito T. Laminar screw fixation in the subaxial cervical spine: A report on three cases. *World J Orthop* 2016; 7(10): 695-699 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i10/695.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i10.695>

INTRODUCTION

Posterior surgical stabilization for instability of the cervical spine can be achieved using various techniques. Traditionally, posterior wiring methods have been used^[1,2]. Recently, methods involving the use of screws and rods, including pedicle^[3], lateral mass^[4], and transarticular screws^[5], have been widely applied because of the resulting biomechanically rigid stabilization. However, screw insertion is associated with a high risk of injury to the vertebral artery because of differences in the position of the foramen transversarium of the cervical spine, the size of the pedicle of the vertebral arch, and the course of the vertebral arteries among patients. Furthermore, the malposition of these screws can cause serious complications, including massive hemorrhage, neurological deficits, and possible death^[6-8]. Here, we describe a novel fixation method involving the use of laminar screws in the subaxial spine for posterior fusion of the cervical spine.

CASE REPORT

Case 1

A 32-year-old man with neck pain had an asymptomatic dumbbell-shaped schwannoma with highly destructive changes observed on radiography (Figure 1). Preoperative magnetic resonance imaging (MRI) showed narrowing of the right vertebral artery due to pressure from the tumor. Subsequently, tumor resection was performed using a posterior approach with total facetectomies of the right C2-3 through C6-7 levels. Reconstruction was achieved using C2-C6 laminar screw fixation (3.5 mm in diameter); the screws were placed in the left lamina to avoid injuring the vertebral artery on the dominant side. Minimal canal invasion by the screw at the C6 level without any resulting neurological deficit was noted. The remaining screws were appropriately placed (Figure 1).

The patient's post-surgical course was uneventful. At 5 years postoperatively, his neck pain disappeared and solid bone fusion was achieved with no instrumentation failure (Figure 1).

Case 2

A 15-year-old girl had a Ewing's sarcoma that involved the right C7 and C8 nerve roots. She began to feel right arm numbness at 12 years of age, and she was diagnosed with a cervical tumor on MRI. In the same year, hemilaminectomy of the right C6 and C7 levels, medial facetectomies of the right C6-7 and Th1 levels, and tumor resection were performed. Pathology of the resected tissues confirmed Ewing's sarcoma. Postoperatively, chemotherapy and radiotherapy were

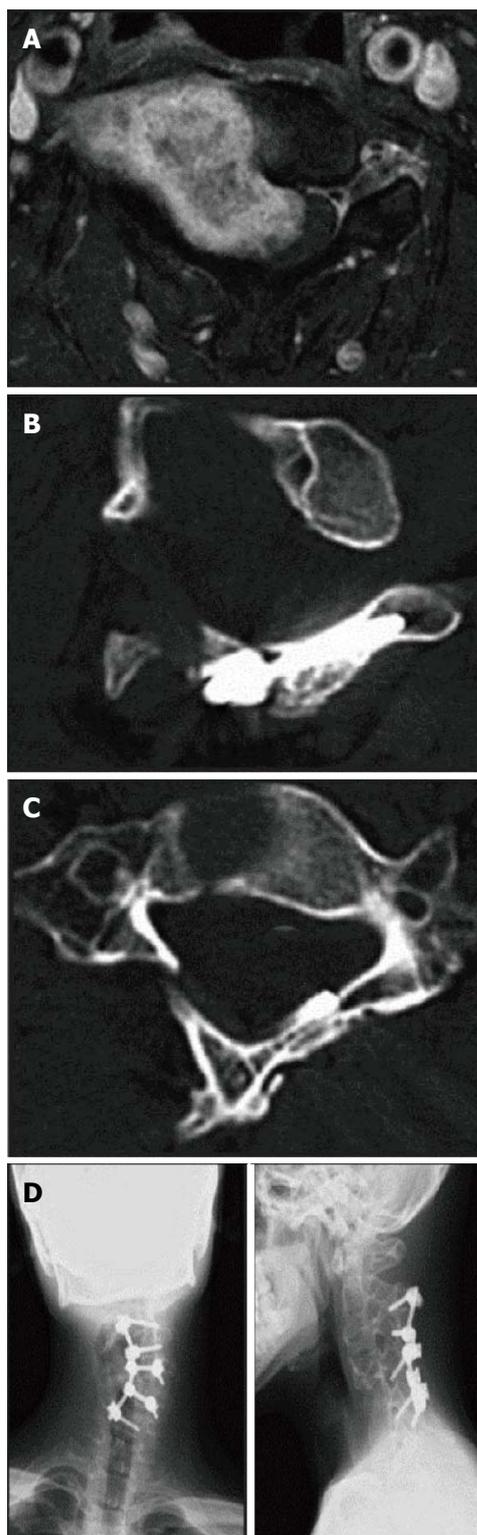


Figure 1 Case 1. A: A magnetic resonance imaging scan image showing a dumbbell-shaped schwannoma at the C3 level; B, C: Computed tomography images showing an appropriately inserted C4 laminar screw (B) and a C6 laminar screw with minimal canal invasion (C); D: A roentgenogram showing solid bone fusion after C2-6 laminar screw fixation.

repeated.

Two years postoperatively, recurrence of the tumor was detected on MRI. However, no neurological deficits

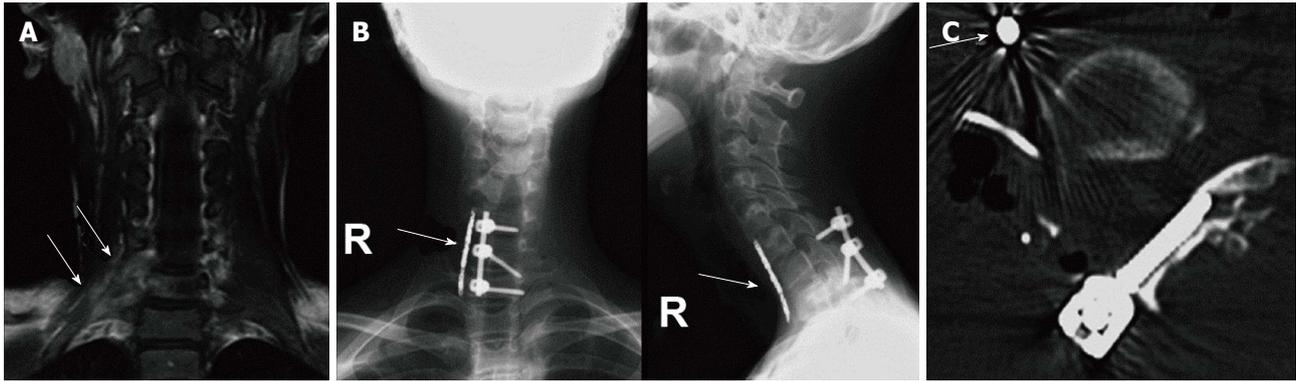


Figure 2 Case 2. A: A magnetic resonance imaging scan image showing a Ewing's sarcoma involving the right C7 and C8 nerve roots (arrows); B: Roentgenograms showing the laminar screws, which are placed at the C6–Th1 levels with a preoperative embolic coil in the right vertebral artery (arrows); C: A computed tomography image showing a C6 laminar screw penetrating the facet joint and a preoperative embolic coil (arrows).

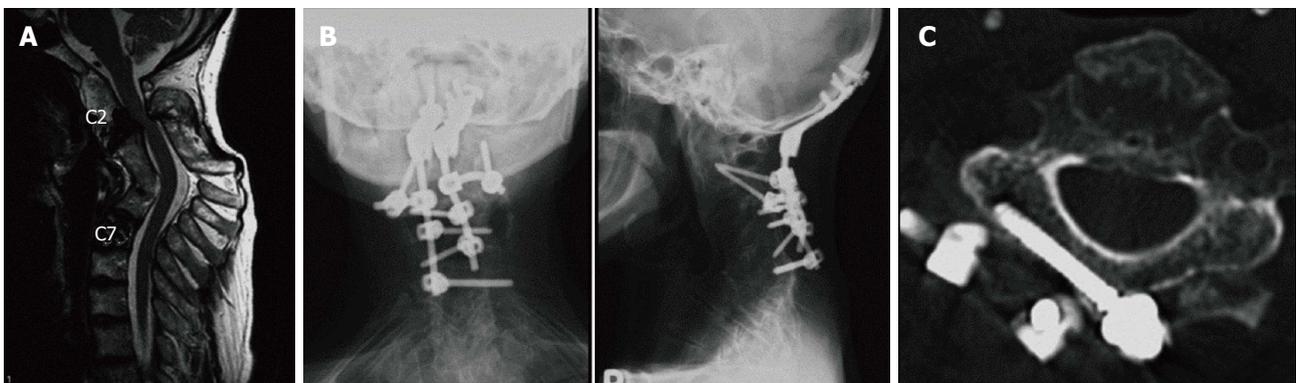


Figure 3 Case 3. A: A magnetic resonance imaging scan image showing severe cervical kyphosis with junctional canal stenosis at the C2-3 levels; B: Roentgenograms showing posterior arthrodesis performed using occipital plates, C2 pedicle screws, and laminar screws at the C3-C6 levels; C: A computed tomography image showing an appropriately inserted C3 laminar screw.

were observed. The tumor was dumbbell-shaped and was located in the intra- and extra-foraminal areas of the C6-7 and C7-Th1 levels (Figure 2). Revision surgery was performed after embolization of the right vertebral artery. Using the posterior approach, laminar screws were inserted at the left C6-Th1 levels to avert the risk of injuring the dominant vertebral artery (Figure 2). Total facetectomies of the right C6-7 and Th1 levels and tumor resection of the right C7 and C8 nerve roots were performed. Additional tumor resection using an anterolateral approach was performed according to the method described by Hodgson^[9].

From the day after the operation, she could walk with a soft neck brace, and she exhibited no neurological deficits other than a dropped finger. Two years after the second operation, recurrence of the tumor was detected, and it was treated with chemotherapy. The laminar screws continued to remain rigidly fixed.

Case 3

A 61-year-old woman experienced neck pain and loss of fine motor control of her hand, and 1 year later, she was referred to our hospital for treatment. She had a history of tuberculosis at 8 years of age, which was

conservatively treated for 4 years. She had cervical myelopathy due to an unstable C2-3 joint with marked kyphosis at the C3-6 levels (Figure 3). Because the laminae were very thick, a laminar screw system was selected for cervical fixation. After decompression with partial laminectomy at the C2-3 level, posterior cervical spinal arthrodesis was performed using occipital plates, C2 pedicles, and laminar screws at the C3-C6 levels (3.5 mm screws) with less exposure outside of the lateral mass.

Postoperatively, the patient was mildly immobilized with a soft neck brace, and her post-surgical course was uneventful. At 4 years postoperatively, her neck pain greatly improved and excellent postoperative stability was noted (Figure 3).

DISCUSSION

Here, we reported a novel fixation method involving the use of practical laminar screws in the subaxial spine. Posterior cervical fixation has often been used for stabilizing the cervical spine, correcting deformities, and easing the symptoms of degenerative diseases. Recently, fixation methods involving screws and rods

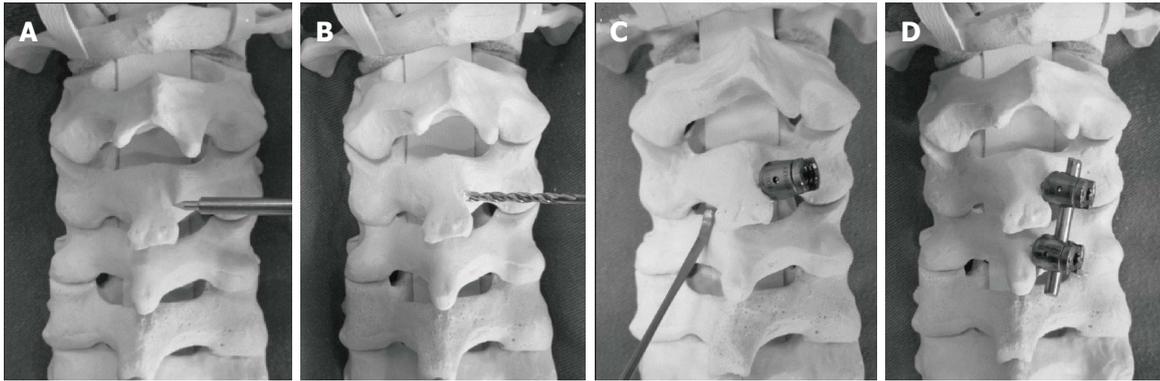


Figure 4 Surgical procedures. A: Create a small cortical window at the junction of the C3 spinous process and the lamina on the right; B: Using a hand drill, carefully drill along the length of the contralateral (left lamina), with the drill visually aligned among the angle of the exposed contralateral laminar surface; C: Insert a 3.5 mm diameter polyaxial screw along the same trajectory in the left C3 lamina. Palpate the ventral lamina with a Penfield dissector to verify that no cortical breakthrough into the spinal canal has occurred; D: Using the same technique as above, insert a 3.5 mm diameter polyaxial screw into the left C4 lamina. Place appropriate rods into the screw heads and attach to C3 and C4 screws.

have become standard, because greater advantages with regard to stabilization and fusion rates of the posterior cervical spine were noted with screw fixation methods than with posterior wiring methods^[3,10-12].

Although cervical pedicle screws are the most biomechanically stable screws^[13], their use requires an advanced surgical technique and they are associated with the risk of neurovascular complications^[14]. To prevent injuring the vertebral artery, pedicle screws should not be used in cases involving the dominant side (*e.g.*, cases 1 and 2). Although the risk of vertebral arterial injury is lower with lateral mass and transarticular screws than with pedicle screws, lateral mass and transarticular screws are difficult to use after facetectomy. Moreover, unilateral use of these screws does not provide sufficient rigidity.

A laminar screw method, which was first reported by Wright^[15] in 2004, uses two screws that are inserted crosswise into the lamina of the axis to prevent vertebral artery injuries and safely perform fixation. Although some authors have reported the use of this method in the subaxial lamina of C7^[16-18], only two previous studies are present on the use of laminar screws elsewhere in the cervical spine^[19,20]. These previous studies did not report sufficient rigidity because thin 1.6 or 2.0 mm mini-screws^[19] were used with a mini-plate for fixing the open lamina at the C3-6 levels or an auxiliary laminar screw^[20] was inserted at the tip of the C3 lamina accompanied with rigid bilateral C1 lateral mass screws. To our knowledge, our case report is the first to describe the use of practical laminar screws in the subaxial cervical spine. Surgical procedures of subaxial laminar screwing are illustrated in Figure 4.

This new laminar screw technique has four advantages. First, it precludes the risk to the vertebral artery, because the path of the screw is present only in the posterior elements. Second, it is less invasive because of the limited lateral cervical exposure. Third, biomechanical stability with laminar screws is similar to that with pedicle screws, as determined previously by the measurement

of pullout forces^[16]. Additionally, surgeons can obtain good rigidity by penetrating the facet joints as shown in cases 1 and 2, and using laminar screws with lateral mass screws as shown in case 3. Fourth, intraoperative navigation systems are not needed, because the screws can be inserted into the lamina under direct vision.

Nakanishi *et al.*^[21] have pointed out that the laminar screw technique poses a risk to the ventrally located spinal canal that is not easily observed. However, we believe that this risk may be reduced by using a Penfield dissector to detect canal violation following the removal of the flavum ligaments between the laminae. Another disadvantage is that laminar screws with a diameter of 3.5 mm cannot be used at the C3-7 levels in all patients. Cardoso *et al.*^[16] measured the diameter of the vertebral arch using a computed tomography (CT) navigation system and reported that the insertion of screws with a diameter of 3 mm was only possible in 2%-39% of male and 0%-26% of female patients at the C3-7 cervical spine^[21]. However, other authors reported significantly greater C7 laminar thickness with caliper measurements than CT measurements. Therefore, the underestimation of laminar thickness using CT may provide a margin of safety when placing screws into laminae that measure close to 3.5 mm on CT.

Preoperative measurements of the laminar diameter and evaluation of the vertebral arteries by using CT and magnetic resonance angiography are important. We believe that the use of laminar screws in the subaxial cervical spine is a viable salvage option for cases that have failed pedicle screw fixation. The accumulation of further data from the treatment of additional cases is required to clarify the indications for and limitations of using the laminar screw technique at the C3-6 levels.

In conclusion, the findings in our cases suggest that the use of the laminar screw technique in the subaxial cervical spine is feasible, as it provides sufficient spinal rigidity. Laminar screws are considered useful for avoiding arterial injuries, and the laminar screw technique is a viable salvage technique.

COMMENTS

Case characteristics

Three cases are discussed with reports of posterior surgical stabilization for instability of the cervical spine.

Clinical diagnosis

Tumor was diagnosed for the first two cases. Cervical myelopathy was the clinical diagnosis for the third case.

Imaging diagnosis

Magnetic resonance imaging was done to for all cases to establish the cause of the problem.

Pathological diagnosis

Pathology analysis was conducted for the 15-year-old female case for confirming the diagnosis of Ewing's sarcoma.

Treatment

For the first case, a 32-year-old male, tumor resection was performed and reconstruction was done using screw fixation. For the 15-year-old female case, tumor resection was performed and postoperatively chemotherapy and radiotherapy was performed. For the 61-year-old female case, cervical fixation was done.

Experiences and lessons

A novel fixation method has been reported with use of practical laminar screws in the subaxial cervical spine. This method reduces the risk to the vertebral artery, is less invasive, provides biomechanical stability and the screws can be inserted with direct vision. Additional cases are needed to clarify the indications and limitations for using laminar screw technique.

Peer-review

This is a good case report with medium term result in one patient and will add to the body of literature for posterior cervical fusion.

REFERENCES

- 1 **Brooks AL**, Jenkins EB. Atlanto-axial arthrodesis by the wedge compression method. *J Bone Joint Surg Am* 1978; **60**: 279-284 [PMID: 348703]
- 2 **Dickman CA**, Sonntag VK, Papadopoulos SM, Hadley MN. The interspinous method of posterior atlantoaxial arthrodesis. *J Neurosurg* 1991; **74**: 190-198 [PMID: 1988587 DOI: 10.3171/jns.1991.74.2.0190]
- 3 **Abumi K**, Itoh H, Taneichi H, Kaneda K. Transpedicular screw fixation for traumatic lesions of the middle and lower cervical spine: description of the techniques and preliminary report. *J Spinal Disord* 1994; **7**: 19-28 [PMID: 8186585 DOI: 10.1097/00002517-199407010-00003]
- 4 **Taniguchi M**, Maruo S. Posterior Lower Cervical Spine Arthrodesis with Lateral Mass Fixation. *Spine & Spinal Cord* 1998; **11**: 217-224
- 5 **Jeanneret B**, Magerl F. Primary posterior fusion C1/2 in odontoid fractures: indications, technique, and results of transarticular screw fixation. *J Spinal Disord* 1992; **5**: 464-475 [PMID: 1490045 DOI: 10.1097/00002517-199212000-00012]
- 6 **Coric D**, Branch CL, Wilson JA, Robinson JC. Arteriovenous fistula as a complication of C1-2 transarticular screw fixation. Case report and review of the literature. *J Neurosurg* 1996; **85**: 340-343 [PMID: 8755766 DOI: 10.3171/jns.1996.85.2.0340]
- 7 **Madawi AA**, Casey AT, Solanki GA, Tuite G, Veres R, Crockard

- 8 **HA**. Radiological and anatomical evaluation of the atlantoaxial transarticular screw fixation technique. *J Neurosurg* 1997; **86**: 961-968 [PMID: 9171174 DOI: 10.3171/jns.1997.86.6.0961]
- 8 **Wright NM**, Laurysen C. Vertebral artery injury in C1-2 transarticular screw fixation: results of a survey of the AANS/CNS section on disorders of the spine and peripheral nerves. American Association of Neurological Surgeons/Congress of Neurological Surgeons. *J Neurosurg* 1998; **88**: 634-640 [PMID: 9525707 DOI: 10.3171/foc.1998.4.2.2]
- 9 **Hodgson AR**. An approach to the cervical spine (C-3 TO C-7). *Clin Orthop Relat Res* 1965; **39**: 129-134 [PMID: 14288168 DOI: 10.1097/00003086-196500390-00012]
- 10 **An HS**, Gordin R, Renner K. Anatomic considerations for plate-screw fixation of the cervical spine. *Spine (Phila Pa 1976)* 1991; **16**: S548-S551 [PMID: 1801270 DOI: 10.1097/00007632-199110001-00019]
- 11 **Harris BM**, Hilibrand AS, Nien YH, Nachwalter R, Vaccaro A, Albert TJ, Siegler S. A comparison of three screw types for uncortical fixation in the lateral mass of the cervical spine. *Spine (Phila Pa 1976)* 2001; **26**: 2427-2431 [PMID: 11707704 DOI: 10.1097/00007632-200111150-00006]
- 12 **Ludwig SC**, Kramer DL, Vaccaro AR, Albert TJ. Transpedicle screw fixation of the cervical spine. *Clin Orthop Relat Res* 1999; **(359)**: 77-88 [PMID: 10078131 DOI: 10.1097/00003086-199902000-00009]
- 13 **Jones EL**, Heller JG, Silcox DH, Hutton WC. Cervical pedicle screws versus lateral mass screws. Anatomic feasibility and biomechanical comparison. *Spine (Phila Pa 1976)* 1997; **22**: 977-982 [PMID: 9152447 DOI: 10.1097/00007632-1997051010-00009]
- 14 **Taneichi H**. Placement technique of cervical screws and prevention of its complications. *Spine & Spinal Cord* 2005; **18**: 1043-1052
- 15 **Wright NM**. Posterior C2 fixation using bilateral, crossing C2 laminar screws: case series and technical note. *J Spinal Disord Tech* 2004; **17**: 158-162 [PMID: 15260101 DOI: 10.1097/00024720-200404000-00014]
- 16 **Cardoso MJ**, Dmitriev AE, Helgeson MD, Stephens F, Campbell V, Lehman RA, Cooper P, Rosner MK. Using lamina screws as a salvage technique at C-7: computed tomography and biomechanical analysis using cadaveric vertebrae. Laboratory investigation. *J Neurosurg Spine* 2009; **11**: 28-33 [PMID: 19569937 DOI: 10.3171/2009.3.SPINE08648]
- 17 **Hong JT**, Yi JS, Kim JT, Ji C, Ryu KS, Park CK. Clinical and radiologic outcome of laminar screw at C2 and C7 for posterior instrumentation--review of 25 cases and comparison of C2 and C7 intralaminar screw fixation. *World Neurosurg* 2010; **73**: 112-118; discussion e15 [PMID: 20860937 DOI: 10.1016/j.wneu.2009.06.010]
- 18 **Şenoğlu M**, Özkan F, Çelik M. Placement of C-7 intralaminar screws: a quantitative anatomical and morphometric evaluation. *J Neurosurg Spine* 2012; **16**: 509-512 [PMID: 22339053 DOI: 10.3171/2012.1.SPINE111048]
- 19 **Hong JT**, Sung JH, Son BC, Lee SW, Park CK. Significance of laminar screw fixation in the subaxial cervical spine. *Spine (Phila Pa 1976)* 2008; **33**: 1739-1743 [PMID: 18628706 DOI: 10.1097/BRS.0b013e31817d2aa2]
- 20 **Jea A**, Johnson KK, Whitehead WE, Luerssen TG. Translaminar screw fixation in the subaxial pediatric cervical spine. *J Neurosurg Pediatr* 2008; **2**: 386-390 [PMID: 19035682 DOI: 10.3171/PED.2008.2.12.386]
- 21 **Nakanishi K**, Tanaka M, Sugimoto Y, Misawa H, Takigawa T, Fujiwara K, Nishida K, Ozaki T. Application of laminar screws to posterior fusion of cervical spine: measurement of the cervical vertebral arch diameter with a navigation system. *Spine (Phila Pa 1976)* 2008; **33**: 620-623 [PMID: 18344855 DOI: 10.1097/BRS.0b013e318166aa76]

P- Reviewer: Guerado E, Sarda P **S- Editor:** Qiu S **L- Editor:** A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 November 18; 7(11): 700-775



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 329 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), **Cyprus (1)**, Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (17), and United States (65).

EDITOR-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

ASSOCIATE EDITOR

Wasim S Khan, *London*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Taichung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarn, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Taichung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Moraes Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*
Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Bao-Gan Peng, *Beijing*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srecko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*

Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efsthios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiyah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*
 Keith Baldwin, *Philadelphia*

Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort Sam Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

REVIEW

- 700 Ankle arthrodesis: A systematic approach and review of the literature
Yasui Y, Hannon CP, Seow D, Kennedy JG
- 709 Depression and psychiatric disease associated with outcomes after anterior cruciate ligament reconstruction
Wu HH, Liu M, Dines JS, Kelly JD, Garcia GH

MINIREVIEWS

- 718 Management of syndesmotic injuries: What is the evidence?
Schnetzke M, Vetter SY, Beisemann N, Swartman B, Grützner PA, Franke J
- 726 Vitamin D and spine surgery
Mabey T, Singhatanadgige W, Yingsakmongkol W, Limthongkul W, Honsawek S

ORIGINAL ARTICLE

Basic Study

- 731 Three-dimensional reconstructed magnetic resonance scans: Accuracy in identifying and defining knee meniscal tears
Kruger N, McNally E, Al-Ali S, Rout R, Rees JL, Price AJ

Retrospective Cohort Study

- 738 Prosthetic design of reverse total shoulder arthroplasty contributes to scapular notching and instability
Huri G, Familiari F, Salari N, Petersen SA, McFarland EG
- 746 Return to physical activity after gastrocnemius recession
Tang Qian Ying C, Lai Wei Hong S, Lee BH, Thevendran G

Retrospective Study

- 752 Improvements after mod Quad and triangle tilt revision surgical procedures in obstetric brachial plexus palsy
Nath RK, Somasundaram C

Randomized Controlled Trial

- 758 Stochastic resonance whole body vibration increases perceived muscle relaxation but not cardiovascular activation: A randomized controlled trial
Elfering A, Burger C, Schade V, Radlinger L

SYSTEMATIC REVIEWS

- 766 Spinal gout: A review with case illustration
Elgafy H, Liu X, Herron J

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Nathan Joseph Fanter, MD, Attending Doctor, Surgeon, Department of Orthopaedic Surgery, Edward Hines Jr. VA Hospital, Hines, IL 60141, United States

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central, and Scopus.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Xin Kong*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL BOARD MEMBERS
 All editorial board members resources online at <http://www.wjgnet.com/2218-5836/editorialboard.htm>

www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
 Xiu-Xia Song, Director
 Fang-Fang Ji, Vice Director
World Journal of Orthopedics
 Baishideng Publishing Group Inc
 8226 Regency Drive, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

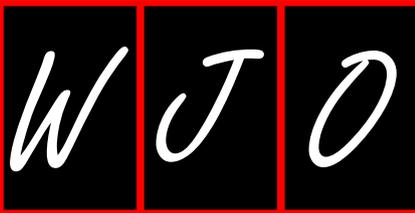
PUBLICATION DATE
 November 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>



Ankle arthrodesis: A systematic approach and review of the literature

Youichi Yasui, Charles P Hannon, Dexter Seow, John G Kennedy

Youichi Yasui, Charles P Hannon, Dexter Seow, John G Kennedy, Hospital for Special Surgery, New York, NY 10021, United States

Youichi Yasui, Charles P Hannon, Dexter Seow, Department of Orthopaedic Surgery, 2nd Teikyo University School of Medicine, Tokyo 1738606, Japan

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: Kennedy JG is a consultant who has received research support from the Ohnell Family Foundation.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: John G Kennedy, MD, MCh, MMSc, FRCS (Orth), Hospital for Special Surgery, 523 East 72nd Street, Suite 507, New York, NY 10021, United States. kennedyj@hss.edu
Telephone: +1-646-7978880
Fax: +1-646-7978966

Received: May 16, 2016
Peer-review started: May 16, 2016
First decision: July 11, 2016
Revised: August 23, 2016
Accepted: September 13, 2016
Article in press: September 18, 2016
Published online: November 18, 2016

Abstract

Ankle arthrodesis is a common treatment used for patients with end-stage ankle arthritis (ESAA). The surgical goal of ankle arthrodesis is to obtain bony union between the tibia and talus with adequate alignment [slight valgus (0°-5°)], neutral dorsiflexion, and slight external rotation positions) in order to provide a pain-free plantigrade foot for weightbearing activities. There are many variations in operative technique including deferring approaches (open or arthroscopic) and differing fixation methods (internal or external fixation). Each technique has its advantage and disadvantages. Success of ankle arthrodesis can be dependent on several factors, including patient selection, surgeons' skills, patient comorbidities, operative care, *etc*. However, from our experience, the majority of ESAA patients obtain successful clinical outcomes. This review aims to outline the indications and goals of arthrodesis for treatment of ESAA and discuss both open and arthroscopic ankle arthrodesis. A systematic step by step operative technique guide is presented for both the arthroscopic and open approaches including a postoperative protocol. We review the current evidence supporting each approach. The review finishes with a report of the most recent evidence of outcomes after both approaches and concerns regarding the development of hindfoot arthritis.

Key words: Ankle; Osteoarthritis; Arthrodesis; Review; Ankle fusion

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Ankle arthrodesis is an effective treatment option for end stage arthritis. There is no current consensus on the most optimal approach and fixation method. It is thus important for the surgeon to understand both the open and arthroscopic approach and when each approach is indicated. Joint alignment must be slightly valgus (0°-5°), neutrally dorsiflexed and slightly in an externally rotated

position. Limb length discrepancies should also be minimal (less than 2.5 cm or 1.0 inch). Failure to address these biomechanical aspects may result in pain and an altered gait pattern. The importance of adequate preoperative forefoot balance cannot be understated to allow for successful postoperative mobility. When performed according to these principles ankle arthrodesis leads to functional improvement and adequate joint fusion in patients with end stage arthritis.

Yasui Y, Hannon CP, Seow D, Kennedy JG. Ankle arthrodesis: A systematic approach and review of the literature. *World J Orthop* 2016; 7(11): 700-708 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/700.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.700>

INTRODUCTION

Ankle arthrodesis and ankle arthroplasty are the two common operative treatments used in end stage ankle arthritis (ESAA)^[1,2]. Recent clinical evidence suggests that ankle arthroplasty leads to superior functional outcomes over ankle arthrodesis^[3-7]. However, ankle arthroplasty is associated with higher rates of postoperative complications and revision surgeries^[3-8]. Despite the increasing popularity of ankle arthroplasty, a large database has indicated that ankle arthrodesis still remains the most common surgical treatment for ESAA^[9,10].

There are several operative techniques for ankle arthrodesis including open or arthroscopic approaches^[11-15]. Although successful clinical outcome can be achieved following both approaches^[11-15], reported outcomes have varied and are conflicted^[16]. The differences in techniques, surgeon skill, patient selection and populations, and outcome measurements utilized all contribute to the variability in outcome after arthrodesis. Ankle arthrodesis should be performed judiciously in young patients, highly active patients, and patients with advanced foot and ankle deformity.

The purpose of this manuscript is to provide: (1) to provide an evidence-based review of ankle arthrodesis for ESAA; and (2) to describe a standardized approach to both open and arthroscopic ankle arthrodesis.

INDICATIONS AND GOALS OF ARTHRODESIS

Ankle arthrodesis is indicated for patients with ESAA that failed a minimum of 3 mo of conservative treatment. The goal of ankle arthrodesis is to provide a pain-free plantigrade foot during weightbearing activities^[17]. Alignment following ankle arthrodesis must be slight valgus (0°-5°), neutral dorsiflexion, and slightly externally rotation. Equinus position of the ankle joint can accompany

genu recurvatum and a varus position of hindfoot can develop painful callosities to the lateral forefoot^[18], which may cause hindfoot pain^[19,20]. Additionally, the surgeon should attempt to minimize limb length discrepancies (less than 2.5 cm or 1.0 inch)^[21-23]. Limb length discrepancies can result in a symptomatic malalignment with altered gait pattern^[24].

Arthroscopic ankle arthrodesis is typically reserved for patients with little to no joint deformity (less than 15° of varus or valgus in the coronal plane). Open arthrodesis is best utilized for patients with moderate to severe deformity as this allows for better visualization for malalignment correction. Additionally, as fusion of the ankle joint will inevitably lead to a lack of motion, preoperative balance of the forefoot is essential. Therefore, careful examination of forefoot balance without excessive pronation or supination is needed^[25]. Arthroscopic or open debridement with subsequent external fixation would be preferred by the authors in patients with significant malalignment, comprised skin, limbs discrepancies, and active/previous infection.

TYPES OF ANKLE ARTHRODESIS

Numerous surgical techniques for ankle arthrodesis have been described^[11-15]. The technique should be selected based on patient characteristics, function and goal of treatment, as well as the preference of the surgeon.

Approach

The approach to ankle arthrodesis is broadly divided into open and arthroscopic techniques. The open approach is further subdivided into the anterior approach, posterior approach, lateral approach, medial approach, and combined medial and lateral approach. Compared with the arthroscopic approach, the main benefit of an open approach includes less difficulty in correcting malalignment, and ease in applying plates and bone grafts. However, open arthrodesis is associated with higher rates of wound complications due to the extensive amount of soft tissue dissection required^[3-7]. This can subsequently lead to longer hospitalization and recovery. Therefore, open approaches are generally reserved for patients with moderate to severe ankle deformities with healthy skin.

Arthroscopic ankle arthrodesis is as a less invasive procedure enabling shorter operative time with comparable union rates^[26-28]. This procedure is most commonly performed using anterior ankle arthroscopy, however recent studies have suggested that posterior ankle arthroscopic arthrodesis may provide better fusion rates^[29]. Arthroscopic ankle arthrodesis is indicated for patients with minimal ankle joint deformity (less than 15° of varus or valgus in coronal plane) or patients who are at higher risk of wound complications (*e.g.*, immunosuppressed, diabetics, rheumatoid arthritis patients). Although arthroscopic arthrodesis is increasingly becoming popular, open ankle arthrodesis remains the mainstay procedure

Table 1 Open ankle arthrodesis

Investigator	Year	Method	No. of patients	Union rate	Outcome(s)
Charnley <i>et al</i> ^[51]	1951	Charnley compression	19	79%	N/A
Boobbyer ^[52]	1981	Internal and external fixation	37	84%	N/A
Kenzora <i>et al</i> ^[53]	1986	External fixation	26	69%	N/A
Sowa <i>et al</i> ^[54]	1989	Compression blade plate	17	94%	10 excellent; 2 good; 2 fair (out of 14; Mazur)
Helm <i>et al</i> ^[55]	1990	Charnley compression	47	85%	N/A
Mann <i>et al</i> ^[11]	1991	Screws from talus to tibia	18	94%	N/A
Kitaoka <i>et al</i> ^[56]	1992	External fixation and bone graft	26	77%	N/A
Wang <i>et al</i> ^[57]	1993	T plate on lateral side	11	91%	N/A
Chen <i>et al</i> ^[58]	1996	Cross screws	40	95%	N/A
Patterson <i>et al</i> ^[59]	1997	Anterior sliding graft with screws	27	93%	N/A
Levine <i>et al</i> ^[44]	1997	Internal fixation and bone graft	22	92%	N/A
Mann <i>et al</i> ^[12]	1998	Internal fixation and fibular graft	81	88%	74 (AOFAS)
Dereymaeker <i>et al</i> ^[60]	1998	Internal and external fixation	14	64%	N/A
Ben-Amor <i>et al</i> ^[61]	1999	80% internal fixation, 20% external fixation	36	97%	56.2 (Duquennoy)
Takakura <i>et al</i> ^[62]	1999	Anterior sliding graft with screws	43	93%	77.9 (Takakura)
Coester <i>et al</i> ^[20]	2001	Internal or external fixation	23	N/A	27 limitation, 38 pain, 47 disability (Foot Function Index)
Bertrand <i>et al</i> ^[63]	2001	84% internal fixation, 16% external fixation	23	87%	69.7 (Duquennoy)
Anderson <i>et al</i> ^[64]	2002	Internal and external fixation	29	89%	N/A
Fuchs <i>et al</i> ^[65]	2003	22% internal fixation, 78% external fixation	18	95%	59.4 (Olerud and Molander)
Buchner <i>et al</i> ^[66]	2003	38% internal fixation, 62% external fixation	45	92%	73.6 (AOFAS)
Kopp <i>et al</i> ^[67]	2004	Internal fixation with staples and screws	41	93%	72.8 (Mazur)
Kennedy <i>et al</i> ^[16]	2006	Internal fixation with screws	41	95%	80.6 (AOFAS)
Thomas <i>et al</i> ^[39]	2006	Internal fixation with transfibular approach	26	100	74 (AOFAS)
Trichard <i>et al</i> ^[68]	2006	60% internal fixation, 40% external fixation	25	N/A	64.7 (Duquennoy)
Smith <i>et al</i> ^[69]	2007	Internal fixation	25	96%	43.7 (AOFAS)
Colman <i>et al</i> ^[70]	2007	Transfibular approach with grafting	48	96%	69 (AOFAS)

for ESAA in the United States of America^[9,10].

Fixation methods

Both internal and external fixation may be used in ankle arthrodesis. Each has its unique advantages; successful outcomes having been demonstrated with both fixation methods^[11-15].

Various methods of internal fixation have been described, including screws, plates, and retrograde intramedullary nails. Many surgeons prefer to use screw fixation as the primary means of internal fixation, because screws are easy to use, have low morbidity (they only require small percutaneous incisions) and are cheaper compared to most other methods. However, higher nonunion rates of the ankle joint have been reported with screw fixation especially in osteoporotic bone^[30,31]. Plates are advantageous for ankle arthrodesis because there are many options when using plates. The surgeon has choices with regard the type of plate needed (e.g., conventional or locking), how many plates and where to place the plates. While some surgeons prefer plates because they are stiffer constructs than screws that may achieve better union rates, the extensive dissection needed to place the plate can lead to a higher risk of infection and morbidity^[32-34]. A combination of plates and screws may also be used. A recent bio-mechanical study found that a combination of plate and screw fixation provided significantly greater stiffness than plates or screws alone. In this study there were no significant difference between 3 compression screws,

anterior plate and lateral plate fixation^[34]. Retrograde intramedullary arthrodesis is typically reserved for arthrodesis of both the ankle and subtalar joints^[35-38]. Patients with ESAA typically have concomitant subtalar arthritis. In these patients, it is difficult to delineate whether the pain is coming solely from the tibiotalar joint, the subtalar joint or a combination of both. The surgeon must determine this preoperatively because it is best to avoid arthrodesis of the subtalar joint whenever possible especially when the ankle will be fused. In the setting of a tibiotalar arthrodesis the subtalar joint is critical for gait stability^[20,39,40]. The subtalar joint allows for inversion and eversion of the ankle joint and therefore, this can compensate for a more stable gait when joint motion is permanently reduced post-arthrodesis.

External fixation is typically indicated for complex patients with significant bone defects, limb length discrepancies, poor bone quality, and active or previous infection^[31]. Overall, union rates and outcomes measures of external fixation are inferior to internal fixation (Table 1).

OPERATIVE TREATMENT

Two standardized methods of ankle arthrodesis for ESAA is described here: Open and arthroscopic. For both methods, the joint is fixed with two or more screws. Patients are placed in a short leg cast and immobilized for 6 wk. Patients have achieved successful outcomes following either approach in our experience^[16].



Figure 1 Lateral transfibular approach.

Open arthrodesis with screw fixation

Patient positioning and equipment: The patient is placed in the supine position with the feet at the edge of the bed. A tourniquet is typically used at the level of the thigh and applied before the start of the case. All equipment should be confirmed prior to the onset of the case. Osteotomes, a bone saw, and curettes are needed for the osteotomy and debridement of the joint surface. A large fragment cannulated drill set and screws (4.0/6.5/7.3 mm) are required to fuse the ankle joint. Fluoroscopy should be used to confirm ankle alignment and screw positions.

Steps of the procedure: (1) Marking anatomical landmarks: Anatomical landmarks are marked using a sterile surgical marker. In this procedure, the lateral malleolus (LM), medial malleolus (MM), ankle joint line, fourth metatarsal, fifth metatarsal, superficial peroneal nerve, and sural nerve are all identified and marked. Then, a hockey-stick-shaped incision is outlined over the lateral aspect of the LM, starting approximately 7.0 cm above the tip of the LM and extending distally to the base of the fourth metatarsal. Additionally, a longitudinal medial skin incision line is marked over medial gutter of ankle joint; (2) Skin incision and osteotomy of distal fibula: The first skin incision is made over the fibula along the previously described outline. Once distal tibiofibular joint is identified, soft tissues including the anterior inferior talofibular ligament, interosseous ligament, and interosseous membrane are resected. An osteotomy of the distal fibula is then made in a beveled fashion approximately 2.5 cm proximal to the ankle joint using a sagittal oscillating saw. The resected bone block (medial side of fibula) should be kept for local autologous bone grafting later on in the case (Figure 1). After the osteotomy is complete, the lateral aspect of the fibula is retracted posteriorly. It is important to preserve the fibula as best as possible to minimize the risk of non-union; (3) Debridement of joint surface cartilage: After the fibular osteotomy, the ankle joint is distracted using a lamina spreader. Any inflammation or scar tissue within the ankle joint is debrided and/or removed carefully to fully expose the joint surface. Careful attention during

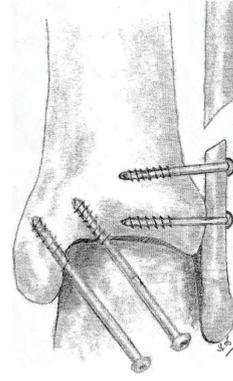


Figure 2 Anteroposterior scheme shows the placement of screws.

exposure of the joint surface is essential to avoid injury to the neurovascular bundle located anterior of the ankle joint capsule. If the full joint surface cannot be visualized at this point, a medial incision with arthrotomy may be needed to reduce the future potential of saphenous nerve damage. After fully exposing the joint surface, cartilage is removed from both the tibia and talus to expose the subchondral bone. The authors prefer to use an osteotome and curette rather than a bone saw or burrs to minimize the risk of thermal necrosis of the subchondral bone. The debridement should also be minimized to maintain joint congruency; (4) Fusion of tibiotalar joint: The tibiotalar joint is fixed typically using two to three 7.3 mm cannulated screws after adequate alignment is obtained. The alignment of tibiotalar joint should be slightly valgus (0° - 5°), neutrally dorsiflexed, and slightly external rotated. The talus should be reduced in a posterior position to obtain the largest possible contact area of joint surfaces. This is to reduce the lever arm of the foot on the mechanical construct. The alignment is evaluated using fluoroscopy in two planes. Two to three guide wires are then inserted in the inferolateral aspect of the base of the talar neck. This technique is similar to what was previously described by Mann *et al*.^[12] The positions of the guide wires should be confirmed using fluoroscopy. Three 7.3 mm cannulated screws are then inserted through the guide wires starting at the talus through the ankle joint and into the tibia. The authors believe that two to three screws are optimal to fuse the joint, as too few screws results in the inadequate compression of the bony surfaces and too many screws reduces the availability of bony surface for osseous integration^[16]; (5) Fusion of lateral malleolus to tibia (Figure 2): Two 4.0 mm screws are used to fix the lateral malleolus and distal tibia into place. Guide wires may be placed before insertion of the screws to ensure adequate alignment. The position of the screws/guide wires should be confirmed with fluoroscopy. Bone graft may be placed around the fusion site to facilitate union. This is especially recommended when there might be factors that could complicate the union such as osteonecrosis of the talus, previous non-union or bony defects^[41-45]. Bone graft can be prepared through the morselization of bone acquired

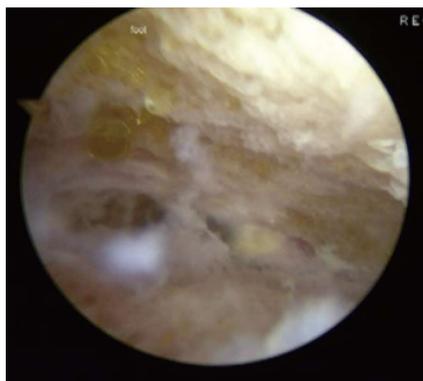


Figure 3 Any remaining cartilage on the tibia, the talus or in the medial or lateral gutters is debrided.

during the distal fibula osteotomy and placed around the site of fusion.

Arthroscopic arthrodesis with screw fixation

Patient positioning and equipment: General arthroscopy equipment is required for an arthroscopic arthrodesis. A 2.7/4.0 mm, 30°/70° arthroscope is typically used. Shavers are required for debridement of soft tissue and for bony resection. A non-invasive distractor and irrigation system are both helpful to obtain good visualization. The fluid pressure is usually set at 50 to 60 mmHg with the fluid flow rate at 0.5 L/min. The ankle joint is fixed using equipment from the large fragment cannulated drill and screw set (6.5 mm). For this procedure, fluoroscopy is necessary.

The patient is placed in the supine position with the ipsilateral hip flexed and supported by a well-padded leg holder. The position of the holder should be proximal to popliteal fossa to avoid constriction of the neurovascular bundle. The ankle and hindfoot is held with a sterile distraction strap.

Steps of the procedure: (1) Marking anatomical landmarks and establishing portals: The careful identification of anatomical landmarks is critical for any arthroscopic procedure of the ankle. The most commonly injured nerve following anterior ankle arthroscopy is the superficial peroneal nerve (up to 2.9%)^[46]. Anterior ankle arthrodesis is performed using anteromedial (AM), anterolateral (AL) and occasionally posterolateral (PL) portals. The lateral malleolus (LM), medial malleolus (MM), peroneus tertius, tibialis anterior tendon (TAT), superficial peroneal nerve, and sural nerve are all identified and marked. At the level of ankle joint, the AM portal is established just medial to the medial border of the TAT and the AL portal is placed lateral to peroneus tertius. The PL portal is marked 1.0 mm anterior to the lateral borders of Achilles tendon with also bring at horizontal level with the inferior pole of the MM and the tip of LM. Arthroscopic portals are created using “nic and spread” technique to decrease the risk of iatrogenic nerve damage. After the skin incision, subcutaneous blunt dissection is performed using a mosquito clamp.

A 2.7 mm arthroscope sleeve with a trocar is then carefully advanced. Once the anterior aspect of tibia can be palpated with the trocar, it is switched out for a 2.7 mm arthroscope. The authors prefer the insertion of portals in the following order: AM portal, AL portal and PL portals; (2) Debridement and exposure: Debridement of the synovium and scar tissue is typically required to improve visualization of the ankle joint surface. Any remaining cartilage on the tibia, the talus or in the medial or lateral gutters is then debrided using a shaver, burr, or curette (Figure 3). To fully visualize the posterior aspect of the joint, the PL portal may need to be utilized. In several previous studies, investigators have suggested that poor debridement of the posterior portion of the ankle joint may compromise ankle fusion rates^[47,48]. Adequate debridement can be assessed by the visualization of blood arising from the subchondral bone of the talus and tibia when inflow pressure is decreased; and (3) Tibiotalar fixation: The tibiotalar joint is fixed typically using two to three large cannulated screws. A Kirschner wire is first inserted 10° to 20° starting at the anterolateral tibia approximately 3 to 4 cm above the joint line and towards the posterior aspect of the horizontal axis of the tibia. A second Kirschner wire is then inserted from the anteromedial aspect of the tibia in a similar orientation aiming toward the central talar dome. These Kirschner wires should be altogether inserted at the tibial joint surface. The location of the Kirschner wires should be confirmed by both arthroscopy (Figure 4A) and fluoroscopy. Following the confirmation of adequate talocrural joint alignment, the wires are then advanced into talus (Figure 4B). Screws are then inserted over these Kirschner wires (Figure 4C). A countersink may be required to reduce the prominence of the screw heads.

BIOLOGICS

Biologics may be used to aid in fusion of the ankle in both the open and arthroscopic techniques. Two types of biologics are currently available: Osteoconductive and osteoinductive agents. Osteoconductive agents, *e.g.*, bone allografts, demineralized bone matrix and various apatitic pastes, are agents that serve as a scaffold at the site of fusion. This scaffold acts as a tissue network to facilitate autologous cell interaction for osteogenesis. Osteoinductive agents, *e.g.*, bone morphogenetic proteins, platelet-rich plasma or concentrated bone marrow aspirate, are agents that directly facilitate osteogenesis. This may be in the form of containing growth factors (platelet-rich plasma) or stem cells (concentrated bone marrow aspirate) to stimulate the formation of osteoblasts. Biologics should be placed into the fusion site before and after the final seating of screws.

POSTOPERATIVE REHABILITATION

The ankle joint is immobilized in a non-weightbearing leg cast for 6 wk. The cast is then removed and



Figure 4 Kirschner wires should be altogether inserted at the tibial joint surface. A: Arthroscopic view shows the location of the Kirschner wires; B: Fluoroscopic view shows location of Kirschner wires; C: Screw fixation.

Table 2 Arthroscopic ankle arthrodesis

Investigator	Year	Method	No. of patients	Union rate	Outcome(s)
Ogilvie-Harris <i>et al</i> ^[71]	1993	Tibiotalar and fibulotalar screws	19	89%	N/A
Dent <i>et al</i> ^[72]	1993	Crossed tibiotalar, charnley clamp	8	100%	N/A
De Vriese <i>et al</i> ^[73]	1994	Arthroscopic arthrodesis	10	70%	N/A
Turan <i>et al</i> ^[74]	1995	Arthroscopic arthrodesis	8 (10 ankles)	100%	N/A
Corso <i>et al</i> ^[75]	1995	Tibiotalar and fibulotalar screws	16	100%	N/A
Crosby <i>et al</i> ^[76]	1996	Arthroscopic arthrodesis	42	93%	N/A
Glick <i>et al</i> ^[77]	1996	Cannulated screws	34	97%	N/A
Jerosch <i>et al</i> ^[78]	1996	Tibiotalar and fibulotalar screws	26	85%	N/A
Cameron <i>et al</i> ^[13]	2000	Arthroscopic arthrodesis	15	100%	N/A
Zvijac <i>et al</i> ^[79]	2002	Arthroscopic arthrodesis	21	95%	N/A
Cannon <i>et al</i> ^[80]	2004	Arthroscopic arthrodesis	36	100%	N/A
Saragas ^[81]	2004	Arthroscopic arthrodesis	26	96%	63.9 (modified AOFAS out of 78 points)
Winson <i>et al</i> ^[25]	2005	Arthroscopic arthrodesis	116 (118 ankles)	92%	N/A
Ferkel <i>et al</i> ^[82]	2005	Arthroscopic arthrodesis	35	97%	73.9 (Mazur)
Gougoulias <i>et al</i> ^[83]	2007	Arthroscopic arthrodesis	74 (78 ankles)	97%	N/A
Dannawi <i>et al</i> ^[84]	2011	Arthroscopic arthrodesis	55	91%	81.5 (Mazur)

the patient is transferred over to a Controlled Ankle Movement Walker Boot. Radiographs should be taken at intervals of 6 wk, 3 mo, 6 mo and 1 year to assess the position of fusion and adequacy of union. A gradual 10% increase every two weeks in weightbearing is advised. However, as soon as complete union is evident on radiographs, patients may be allowed to fully weightbear.

OUTCOMES AFTER ANKLE ARTHRODESIS: A SYSTEMATIC REVIEW

Clinical studies on ankle arthrodesis were searched for on the MEDLINE and EMBASE databases using the terms: (open OR arthroscopic) AND (ankle) AND (arthrodesis OR fusion). The search revealed 463 papers from MEDLINE and 695 papers from EMBASE. The inclusion criteria were: (1) the studies' intervention included the use of arthrodesis; (2) clinical studies; and (3) published in a peer-review journal. Exclusion criteria were: (1) review studies; (2) cadaver studies; and (3) animal studies. This resulted in the inclusion of 26 studies on open ankle arthrodesis and 16 studies on

arthroscopic ankle arthrodesis (Table 2).

Union rate has been shown to be a popular outcome measure following arthrodesis, as indicated by its prevalent use in the current literature. Other popular measures included the AOFAS, Duquenois, Mazur, Takakura, Foot Function Index and Olerud and Molander scoring systems.

The average union rate following open arthrodesis was 89% (range: 64%-100%) and following arthroscopic arthrodesis was 94% (range: 70%-100%). In the cohort of patients in the four comparative studies, the average union rate in the open group was 89% and in the arthroscopic group was 91%. However, in the only comparative study reporting clinical outcomes, Townshend *et al*^[26] demonstrated that clinical outcomes only mildly improved following the use of the arthroscopic technique.

In regards to the effects of ankle arthrodesis on the automobile breaking. Jeng *et al*^[49] demonstrated that ankle arthrodesis can significantly decreased the total break reaction time. However, this delay does not exceed the safe reaction brake timing criteria by the United States Federal Highway. Schwienbacher *et al*^[50]

Table 3 Open vs arthroscopic ankle arthrodesis

Investigator		Year	Method	No. of patients	Union rate	Outcome(s)
Myerson <i>et al</i> ^[28]	Open	1991	Screws from tibia to talus	16	100%	N/A
	Arthroscopic		Cannulated screws	17	94%	
O'Brien <i>et al</i> ^[27]	Open	1999	Open technique	17	82%	N/A
	Arthroscopic		Arthroscopic technique	19	84%	
Nielsen <i>et al</i> ^[85]	Open	2008	Open technique	49	84%	N/A
	Arthroscopic		Arthroscopic technique	58	95%	
Townshend <i>et al</i> ^[26]	Open	2013	Open technique	30	N/A	AOS = 29.2 ± 17.2; SF-36 physical = 38.2 ± 11.8; SF-36 mental = 52.2 ± 12.0
	Arthroscopic		Arthroscopic technique	30		

performed comparative case series in a driving simulator and found that patients receiving ankle arthrodesis had less of an ability to brake under emergency circumstances compared to healthy volunteers.

Relationship between ankle arthrodesis and adjacent-joint arthritis in the hindfoot

The development of adjacent hindfoot arthritis following tibiotalar arthrodesis remains a concern. A recent systematic review by Ling *et al*^[86] investigated the relationship between ankle arthrodesis and adjacent-joint arthritis and demonstrated that there was insufficient evidence to support either that ankle arthrodesis caused adjacent-joint arthritis or that pre-existing joint arthritis could have already existed in those cohort of patients. As the current postulation include that there may be inherent pre-existing adjacent joint arthritis in the majority of patients requiring fusion, no clear consensus can be made on whether ankle arthrodesis can cause or predispose to hindfoot arthritis.

Recently, Yasui *et al*^[9] published a large retrospective cohort study that investigated the postoperative adjacent-joint hindfoot arthritis following ankle arthrodesis. The authors found there was significant higher rate of subsequent adjacent-joint arthrodesis in the open cohort than the arthroscopic cohort (7322 open procedures vs 1152 arthroscopic procedure, reoperation rate: 5.6% vs 2.6%, odds ratio: 2.17, 95% confidence level: 1.49-3.16). Regardless of whether adjacent hindfoot arthritis is present before or develops after arthrodesis the authors believe that these patients more commonly have open procedures. The authors hypothesized that open ankle arthrodesis leads to degenerative OA of the adjacent joints more frequently than does the arthroscopic procedure; or, patients undergoing open ankle arthrodesis develop concurrent degenerative arthritis in the adjacent joints more frequently than does the arthroscopic group. To address this subject, further investigation is necessary (Table 3).

CONCLUSION

Ankle arthrodesis is an effective treatment for ESAA that may be achieved through either the open or arthroscopic

approach. Several fixation options exist, however the authors prefer two to three screws. It is difficult to generate a clear consensus on whether open or arthroscopic arthrodesis should be the mainstay of treatment for ESAA because conflicting evidence currently exists. As the current success of arthrodesis continues to depend on a variety of factors, the current review aims to summarize an up-to-date knowledge for optimizing the outcomes of ankle arthrodesis.

REFERENCES

- 1 Agel J, Coetzee JC, Sangeorzan BJ, Roberts MM, Hansen ST. Functional limitations of patients with end-stage ankle arthrosis. *Foot Ankle Int* 2005; **26**: 537-539 [PMID: 16045844]
- 2 Glazebrook M, Daniels T, Younger A, Foote CJ, Penner M, Wing K, Lau J, Leighton R, Dunbar M. Comparison of health-related quality of life between patients with end-stage ankle and hip arthrosis. *J Bone Joint Surg Am* 2008; **90**: 499-505 [PMID: 18310699 DOI: 10.2106/JBJS.F.01299]
- 3 Haddad SL, Coetzee JC, Estok R, Fahrback K, Banel D, Nalysnyk L. Intermediate and long-term outcomes of total ankle arthroplasty and ankle arthrodesis. A systematic review of the literature. *J Bone Joint Surg Am* 2007; **89**: 1899-1905 [PMID: 17768184 DOI: 10.2106/JBJS.F.01149]
- 4 Daniels TR, Younger AS, Penner M, Wing K, Dryden PJ, Wong H, Glazebrook M. Intermediate-term results of total ankle replacement and ankle arthrodesis: a COFAS multicenter study. *J Bone Joint Surg Am* 2014; **96**: 135-142 [PMID: 24430413 DOI: 10.2106/JBJS.L.01597]
- 5 Krause FG, Windolf M, Bora B, Penner MJ, Wing KJ, Younger AS. Impact of complications in total ankle replacement and ankle arthrodesis analyzed with a validated outcome measurement. *J Bone Joint Surg Am* 2011; **93**: 830-839 [PMID: 21498491 DOI: 10.2106/JBJS.J.00103]
- 6 Jordan RW, Chahal GS, Chapman A. Is end-stage ankle arthrosis best managed with total ankle replacement or arthrodesis? A systematic review. *Adv Orthop* 2014; **2014**: 986285 [PMID: 25215242 DOI: 10.1155/2014/986285]
- 7 SooHoo NF, Zingmond DS, Ko CY. Comparison of reoperation rates following ankle arthrodesis and total ankle arthroplasty. *J Bone Joint Surg Am* 2007; **89**: 2143-2149 [PMID: 17908889 DOI: 10.2106/JBJS.F.01611]
- 8 Schuh R, Hofstaetter J, Krismer M, Bevoni R, Windhager R, Trnka HJ. Total ankle arthroplasty versus ankle arthrodesis. Comparison of sports, recreational activities and functional outcome. *Int Orthop* 2012; **36**: 1207-1214 [PMID: 22173565 DOI: 10.1007/s00264-011-1455-8]
- 9 Yasui Y, Vig KS, Murawski CD, Desai P, Savage-Elliott I, Kennedy JG. Open Versus Arthroscopic Ankle Arthrodesis: A Comparison of Subsequent Procedures in a Large Database. *J Foot*

- Ankle Surg* 2016; **55**: 777-781 [PMID: 27067198 DOI: 10.1053/j.jfas.2016.03.007]
- 10 **Terrell RD**, Montgomery SR, Pannell WC, Sandlin MI, Inoue H, Wang JC, SooHoo NF. Comparison of practice patterns in total ankle replacement and ankle fusion in the United States. *Foot Ankle Int* 2013; **34**: 1486-1492 [PMID: 23774468 DOI: 10.1177/1071100713494380]
 - 11 **Mann RA**, Van Manen JW, Wapner K, Martin J. Ankle fusion. *Clin Orthop Relat Res* 1991; **(268)**: 49-55 [PMID: 2060226]
 - 12 **Mann RA**, Rongstad KM. Arthrodesis of the ankle: a critical analysis. *Foot Ankle Int* 1998; **19**: 3-9 [PMID: 9462906 DOI: 10.1177/107110079801900102]
 - 13 **Cameron SE**, Ullrich P. Arthroscopic arthrodesis of the ankle joint. *Arthroscopy* 2000; **16**: 21-26 [PMID: 10627341 DOI: 10.1016/S0749-8063(00)90123-3]
 - 14 **Wang L**, Gui J, Gao F, Yu Z, Jiang Y, Xu Y, Shen H. Modified posterior portals for hindfoot arthroscopy. *Arthroscopy* 2007; **23**: 1116-1123 [PMID: 17916479 DOI: 10.1016/j.arthro.2007.04.015]
 - 15 **Stone JW**. Arthroscopic ankle arthrodesis. *Foot Ankle Clin* 2006; **11**: 361-368 [PMID: 16798516]
 - 16 **Kennedy JG**, Hodgkins CW, Brodsky A, Bohne WH. Outcomes after standardized screw fixation technique of ankle arthrodesis. *Clin Orthop Relat Res* 2006; **447**: 112-118 [PMID: 16741477 DOI: 10.1097/01.blo.0000203480.04174.0e]
 - 17 **Nihal A**, Gellman RE, Embil JM, Trepman E. Ankle arthrodesis. *Foot Ankle Surg* 2008; **14**: 1-10 [PMID: 19083604 DOI: 10.1016/j.fas.2007.08.004]
 - 18 **Mazur JM**, Schwartz E, Simon SR. Ankle arthrodesis. Long-term follow-up with gait analysis. *J Bone Joint Surg Am* 1979; **61**: 964-975 [PMID: 489661]
 - 19 **Morrey BF**, Wiedeman GP. Complications and long-term results of ankle arthrodesis following trauma. *J Bone Joint Surg Am* 1980; **62**: 777-784 [PMID: 7391101]
 - 20 **Coester LM**, Saltzman CL, Leupold J, Pontarelli W. Long-term results following ankle arthrodesis for post-traumatic arthritis. *J Bone Joint Surg Am* 2001; **83-A**: 219-228 [PMID: 11216683]
 - 21 **Gross RH**. Leg length discrepancy: how much is too much? *Orthopedics* 1978; **1**: 307-310 [PMID: 733195]
 - 22 **Moseley CF**. Leg length discrepancy. *Orthop Clin North Am* 1987; **18**: 529-535 [PMID: 3313161]
 - 23 **Morrissy RT**, Weinstein SL. Lovell and Winter's Pediatric Orthopaedics. 6th edition. Philadelphia (PA): Lippincott Williams & Wilkins, 2006: 1234-1236
 - 24 **Gurney B**, Mermier C, Robergs R, Gibson A, Rivero D. Effects of limb-length discrepancy on gait economy and lower-extremity muscle activity in older adults. *J Bone Joint Surg Am* 2001; **83-A**: 907-915 [PMID: 11407800]
 - 25 **Winson IG**, Robinson DE, Allen PE. Arthroscopic ankle arthrodesis. *J Bone Joint Surg Br* 2005; **87**: 343-347 [PMID: 15773643 DOI: 10.1302/0301-620X.87B3.15756]
 - 26 **Townshend D**, Di Silvestro M, Krause F, Penner M, Younger A, Glazebrook M, Wing K. Arthroscopic versus open ankle arthrodesis: a multicenter comparative case series. *J Bone Joint Surg Am* 2013; **95**: 98-102 [PMID: 23235956 DOI: 10.2106/JBJS.K.01240]
 - 27 **O'Brien TS**, Hart TS, Shereff MJ, Stone J, Johnson J. Open versus arthroscopic ankle arthrodesis: a comparative study. *Foot Ankle Int* 1999; **20**: 368-374 [PMID: 10395339 DOI: 10.1177/107110079902000605]
 - 28 **Myerson MS**, Quill G. Ankle arthrodesis. A comparison of an arthroscopic and an open method of treatment. *Clin Orthop Relat Res* 1991; **(268)**: 84-95 [PMID: 2060232]
 - 29 **Nickisch F**, Barg A, Saltzman CL, Beals TC, Bonasia DE, Phisitkul P, Femino JE, Amendola A. Postoperative complications of posterior ankle and hindfoot arthroscopy. *J Bone Joint Surg Am* 2012; **94**: 439-446 [PMID: 22398738 DOI: 10.2106/JBJS.K.00069]
 - 30 **Thordarson DB**, Markolf KL, Cracchiolo A. Arthrodesis of the ankle with cancellous-bone screws and fibular strut graft. Biomechanical analysis. *J Bone Joint Surg Am* 1990; **72**: 1359-1363 [PMID: 2229113]
 - 31 **Thordarson DB**, Markolf K, Cracchiolo A. Stability of an ankle arthrodesis fixed by cancellous-bone screws compared with that fixed by an external fixator. A biomechanical study. *J Bone Joint Surg Am* 1992; **74**: 1050-1055 [PMID: 1522091]
 - 32 **Nasson S**, Shuff C, Palmer D, Owen J, Wayne J, Carr J, Adelaar R, May D. Biomechanical comparison of ankle arthrodesis techniques: crossed screws vs. blade plate. *Foot Ankle Int* 2001; **22**: 575-580 [PMID: 11503983]
 - 33 **Betz MM**, Benninger EE, Favre PP, Wieser KK, Vich MM, Espinosa N. Primary stability and stiffness in ankle arthrodesis-crossed screws versus anterior plating. *Foot Ankle Surg* 2013; **19**: 168-172 [PMID: 23830164 DOI: 10.1016/j.fas.2013.04.006]
 - 34 **Clifford C**, Berg S, McCann K, Hutchinson B. A biomechanical comparison of internal fixation techniques for ankle arthrodesis. *J Foot Ankle Surg* 2015; **54**: 188-191 [PMID: 25116232 DOI: 10.1053/j.jfas.2014.06.002]
 - 35 **Pinzur MS**, Kelikian A. Charcot ankle fusion with a retrograde locked intramedullary nail. *Foot Ankle Int* 1997; **18**: 699-704 [PMID: 9391814 DOI: 10.1177/107110079701801104]
 - 36 **Pinzur MS**, Noonan T. Ankle arthrodesis with a retrograde femoral nail for Charcot ankle arthropathy. *Foot Ankle Int* 2005; **26**: 545-549 [PMID: 16045846]
 - 37 **Fujimori J**, Yoshino S, Koiwa M, Nakamura H, Shiga H, Nagashima S. Ankle arthrodesis in rheumatoid arthritis using an intramedullary nail with fins. *Foot Ankle Int* 1999; **20**: 485-490 [PMID: 10473058 DOI: 10.1177/107110079902000804]
 - 38 **Moore TJ**, Prince R, Pochatko D, Smith JW, Fleming S. Retrograde intramedullary nailing for ankle arthrodesis. *Foot Ankle Int* 1995; **16**: 433-436 [PMID: 7550958 DOI: 10.1177/107110079501600710]
 - 39 **Thomas R**, Daniels TR, Parker K. Gait analysis and functional outcomes following ankle arthrodesis for isolated ankle arthritis. *J Bone Joint Surg Am* 2006; **88**: 526-535 [PMID: 16510818 DOI: 10.2106/JBJS.E.00521]
 - 40 **Zwipp H**, Rammelt S, Endres T, Heineck J. High union rates and function scores at midterm followup with ankle arthrodesis using a four screw technique. *Clin Orthop Relat Res* 2010; **468**: 958-968 [PMID: 19763726 DOI: 10.1007/s11999-009-1074-5]
 - 41 **Stauffer RN**. Salvage of painful total ankle arthroplasty. *Clin Orthop Relat Res* 1982; **(170)**: 184-188 [PMID: 7127945 DOI: 10.1097/00003086-198210000-00024]
 - 42 **Kitaoka HB**, Patzer GL. Arthrodesis for the treatment of arthrosis of the ankle and osteonecrosis of the talus. *J Bone Joint Surg Am* 1998; **80**: 370-379 [PMID: 9531205]
 - 43 **Kirkpatrick JS**, Goldner JL, Goldner RD. Revision arthrodesis for tibiotalar pseudarthrosis with fibular onlay-inlay graft and internal screw fixation. *Clin Orthop Relat Res* 1991; **(268)**: 29-36 [PMID: 2060221]
 - 44 **Levine SE**, Myerson MS, Lucas P, Schon LC. Salvage of pseudoarthrosis after tibiotalar arthrodesis. *Foot Ankle Int* 1997; **18**: 580-585 [PMID: 9310771 DOI: 10.1177/107110079701800910]
 - 45 **Kitaoka HB**. Salvage of nonunion following ankle arthrodesis for failed total ankle arthroplasty. *Clin Orthop Relat Res* 1991; **(268)**: 37-43 [PMID: 2060224]
 - 46 **Deng DF**, Hamilton GA, Lee M, Rush S, Ford LA, Patel S. Complications associated with foot and ankle arthroscopy. *J Foot Ankle Surg* 2012; **51**: 281-284 [PMID: 22188904 DOI: 10.1053/j.jfas.2011.11.011]
 - 47 **Hendrickx RP**, de Leeuw PA, Golano P, van Dijk CN, Kerkhoffs GM. Safety and efficiency of posterior arthroscopic ankle arthrodesis. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2420-2426 [PMID: 24807231 DOI: 10.1007/s00167-014-3040-3]
 - 48 **Malekpour L**, Rahali S, Duparc F, Dujardin F, Roussignol X. Anatomic Feasibility Study of Posterior Arthroscopic Tibiotalar Arthrodesis. *Foot Ankle Int* 2015; **36**: 1229-1234 [PMID: 26048588 DOI: 10.1177/1071100715587232]
 - 49 **Jeng CL**, Lin JS, Amoyal K, Campbell J, Myerson MS. Driving brake reaction time following right ankle arthrodesis. *Foot Ankle Int* 2011; **32**: 896-899 [PMID: 22097166 DOI: 10.3113/FAI.2011.0896]

- 50 **Schwienbacher S**, Aghayev E, Hofmann UK, Jordan M, Marmotti A, Röder C, Ipach I. Driving and emergency braking may be impaired after tibiotalar joint arthrodesis: conclusions after a case series. *Int Orthop* 2015; **39**: 1335-1341 [PMID: 25947900 DOI: 10.1007/s00264-015-2789-4]
- 51 **Charnley J**. Compression arthrodesis of the ankle and shoulder. *J Bone Joint Surg Br* 1951; **33B**: 180-191 [PMID: 14832316]
- 52 **Boobhyer GN**. The long-term results of ankle arthrodesis. *Acta Orthop Scand* 1981; **52**: 107-110 [PMID: 7211309 DOI: 10.3109/17453678108991769]
- 53 **Kenzora JE**, Simmons SC, Burgess AR, Edwards CC. External fixation arthrodesis of the ankle joint following trauma. *Foot Ankle* 1986; **7**: 49-61 [PMID: 3091461 DOI: 10.1177/107110078600700108]
- 54 **Sowa DT**, Krackow KA. Ankle fusion: a new technique of internal fixation using a compression blade plate. *Foot Ankle* 1989; **9**: 232-240 [PMID: 2731835 DOI: 10.1177/107110078900900505]
- 55 **Helm R**. The results of ankle arthrodesis. *J Bone Joint Surg Br* 1990; **72**: 141-143 [PMID: 2298774]
- 56 **Kitaoka HB**, Anderson PJ, Morrey BF. Revision of ankle arthrodesis with external fixation for non-union. *J Bone Joint Surg Am* 1992; **74**: 1191-1200 [PMID: 1400548]
- 57 **Wang GJ**, Shen WJ, McLaughlin RE, Stamp WG. Transfibular compression arthrodesis of the ankle joint. *Clin Orthop Relat Res* 1993; **(289)**: 223-227 [PMID: 8472421 DOI: 10.1097/00003086-199304000-00034]
- 58 **Chen YJ**, Huang TJ, Shih HN, Hsu KY, Hsu RW. Ankle arthrodesis with cross screw fixation. Good results in 36/40 cases followed 3-7 years. *Acta Orthop Scand* 1996; **67**: 473-478 [PMID: 8948253 DOI: 10.3109/17453679608996671]
- 59 **Patterson BM**, Inglis AE, Moeckel BH. Anterior sliding graft for tibiotalar arthrodesis. *Foot Ankle Int* 1997; **18**: 330-334 [PMID: 9208289 DOI: 10.1177/107110079701800603]
- 60 **Dereymaeker GP**, Van Eygen P, Driesen R, De Ferm A. Tibiotalar arthrodesis in the rheumatoid foot. *Clin Orthop Relat Res* 1998; **(349)**: 43-47 [PMID: 9584365 DOI: 10.1097/00003086-199804000-00006]
- 61 **Ben Amor H**, Kallel S, Karray S, Saadaoui F, Zouari M, Litaïem T, Douik M. [Consequences of tibiotalar arthrodesis on the foot. A retrospective study of 36 cases with 8.5 years of followup]. *Acta Orthop Belg* 1999; **65**: 48-56 [PMID: 10217002]
- 62 **Takakura Y**, Tanaka Y, Sugimoto K, Akiyama K, Tamai S. Long-term results of arthrodesis for osteoarthritis of the ankle. *Clin Orthop Relat Res* 1999; **(361)**: 178-185 [PMID: 10212611 DOI: 10.1097/00003086-199904000-00023]
- 63 **Bertrand M**, Charissoux JL, Mabit C, Arnaud JP. [Tibio-talar arthrodesis: long term influence on the foot]. *Rev Chir Orthop Reparatrice Appar Mot* 2001; **87**: 677-684 [PMID: 11845071]
- 64 **Anderson T**, Montgomery F, Besjakov J, Verdier H, Carlsson A. Arthrodesis of the ankle for non-inflammatory conditions--healing and reliability of outcome measurements. *Foot Ankle Int* 2002; **23**: 390-393 [PMID: 12043981]
- 65 **Fuchs S**, Sandmann C, Skwara A, Chylarecki C. Quality of life 20 years after arthrodesis of the ankle. A study of adjacent joints. *J Bone Joint Surg Br* 2003; **85**: 994-998 [PMID: 14516034 DOI: 10.1302/0301-620X.85B7.13984]
- 66 **Buchner M**, Sabo D. Ankle fusion attributable to posttraumatic arthrosis: a long-term followup of 48 patients. *Clin Orthop Relat Res* 2003; **(406)**: 155-164 [PMID: 12579015 DOI: 10.1097/00003086-200301000-00025]
- 67 **Kopp FJ**, Banks MA, Marcus RE. Clinical outcome of tibiotalar arthrodesis utilizing the chevron technique. *Foot Ankle Int* 2004; **25**: 225-230 [PMID: 15132930]
- 68 **Trichard T**, Remy F, Girard J, Soenen M, Duquenooy A, Migaud H. [Long-term behavior of ankle fusion: assessment of the same series at 7 and 23 year (19-36 years) follow-up]. *Rev Chir Orthop Reparatrice Appar Mot* 2006; **92**: 701-707 [PMID: 17124454 DOI: 10.1016/S0035-1040(06)75931-1]
- 69 **Smith R**, Wood PL. Arthrodesis of the ankle in the presence of a large deformity in the coronal plane. *J Bone Joint Surg Br* 2007; **89**: 615-619 [PMID: 17540746 DOI: 10.1302/0301-620X.89B5.18109]
- 70 **Colman AB**, Pomeroy GC. Transfibular ankle arthrodesis with rigid internal fixation: an assessment of outcome. *Foot Ankle Int* 2007; **28**: 303-307 [PMID: 17371653 DOI: 10.3113/FAI.2007.0303]
- 71 **Ogilvie-Harris DJ**, Lieberman I, Fitisialis D. Arthroscopically assisted arthrodesis for osteoarthrotic ankles. *J Bone Joint Surg Am* 1993; **75**: 1167-1174 [PMID: 8354675]
- 72 **Dent CM**, Patil M, Fairclough JA. Arthroscopic ankle arthrodesis. *J Bone Joint Surg Br* 1993; **75**: 830-832 [PMID: 8376451]
- 73 **De Vriese L**, Dereymaeker G, Fabry G. Arthroscopic ankle arthrodesis. Preliminary report. *Acta Orthop Belg* 1994; **60**: 389-392 [PMID: 7847088]
- 74 **Turan I**, Wredmark T, Felländer-Tsai L. Arthroscopic ankle arthrodesis in rheumatoid arthritis. *Clin Orthop Relat Res* 1995; **(320)**: 110-114 [PMID: 7586812 DOI: 10.1097/00003086-199511000-00018]
- 75 **Corso SJ**, Zimmer TJ. Technique and clinical evaluation of arthroscopic ankle arthrodesis. *Arthroscopy* 1995; **11**: 585-590 [PMID: 8534301 DOI: 10.1016/0749-8063(95)90136-1]
- 76 **Crosby LA**, Yee TC, Formanek TS, Fitzgibbons TC. Complications following arthroscopic ankle arthrodesis. *Foot Ankle Int* 1996; **17**: 340-342 [PMID: 8791081 DOI: 10.1177/107110079601700608]
- 77 **Glick JM**, Morgan CD, Myerson MS, Sampson TG, Mann JA. Ankle arthrodesis using an arthroscopic method: long-term follow-up of 34 cases. *Arthroscopy* 1996; **12**: 428-434 [PMID: 8864000 DOI: 10.1016/S0749-8063(96)90036-5]
- 78 **Jerosch J**, Steinbeck J, Schroder M, Reer R. Arthroscopically assisted arthrodesis of the ankle joint. *Arch Orthop Trauma Surg* 1996; **115**: 182-189 [PMID: 8861587 DOI: 10.1007/BF00434550]
- 79 **Zvijac JE**, Lemak L, Schurhoff MR, Hechtman KS, Uribe JW. Analysis of arthroscopically assisted ankle arthrodesis. *Arthroscopy* 2002; **18**: 70-75 [PMID: 11774145 DOI: 10.1053/jars.2002.29923]
- 80 **Cannon LB**, Brown J, Cooke PH. Early weight bearing is safe following arthroscopic ankle arthrodesis. *Foot Ankle Surg* 2004; **10**: 135-139 [DOI: 10.1016/j.fas.2004.06.001]
- 81 **Saragas N**. Results of arthroscopic arthrodesis of the ankle. *Foot Ankle Surg* 2004; **10**: 141-143 [DOI: 10.1016/j.fas.2004.06]
- 82 **Ferkel RD**, Hewitt M. Long-term results of arthroscopic ankle arthrodesis. *Foot Ankle Int* 2005; **26**: 275-280 [PMID: 15829210]
- 83 **Gougoulias NE**, Agathangelidis FG, Parsons SW. Arthroscopic ankle arthrodesis. *Foot Ankle Int* 2007; **28**: 695-706 [PMID: 17592700 DOI: 10.3113/FAI.2007.0695]
- 84 **Dannawi Z**, Nawabi DH, Patel A, Leong JJ, Moore DJ. Arthroscopic ankle arthrodesis: are results reproducible irrespective of pre-operative deformity? *Foot Ankle Surg* 2011; **17**: 294-299 [PMID: 22017906 DOI: 10.1016/j.fas.2010.12.004]
- 85 **Nielsen KK**, Linde F, Jensen NC. The outcome of arthroscopic and open surgery ankle arthrodesis: a comparative retrospective study on 107 patients. *Foot Ankle Surg* 2008; **14**: 153-157 [PMID: 19083634 DOI: 10.1016/j.fas.2008.01.003]
- 86 **Ling JS**, Smyth NA, Fraser EJ, Hogan MV, Seaworth CM, Ross KA, Kennedy JG. Investigating the relationship between ankle arthrodesis and adjacent-joint arthritis in the hindfoot: a systematic review. *J Bone Joint Surg Am* 2015; **97**: 513-520 [PMID: 25788309 DOI: 10.2106/JBJS.N.00426]

P- Reviewer: Schwienbacher S, Shah NS, Vallejo RBD, Zhang X
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Lu YJ



Depression and psychiatric disease associated with outcomes after anterior cruciate ligament reconstruction

Hao-Hua Wu, Max Liu, Joshua S Dines, John D Kelly, Grant H Garcia

Hao-Hua Wu, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, United States

Hao-Hua Wu, Jordan Medical Education Center, Philadelphia, PA 19104, United States

Max Liu, Stanford School of Medicine, Palo Alto, CA 94305, United States

Joshua S Dines, Grant H Garcia, Hospital for Special Surgery, New York, NY 10021, United States

John D Kelly, Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA 19104, United States

Author contributions: Wu HH, Liu M and Garcia GH helped review the literature for this article and wrote and edited all aspects of the manuscript; Dines JS and Kelly JD designed the study, wrote and edited all aspects of the manuscript.

Conflict-of-interest statement: Joshua S. Dines has received fees for serving as a speaker for Arthrex, Biomet and CONMED Linvatec. Dr. Dines serves on the editorial or governing board of American Journal of Orthopedics and Journal of Shoulder and Elbow Surgeons. Dr. Dines serves as a Board or committee member for the American Shoulder and Elbow Surgeons. Dr. Dines. Receives publishing royalties from Wolters Kluwer Health - Lippincott Williams and Wilkins. John D Kelly IV has received publishing royalties from Springer and SLACK Incorporated. Dr. Kelly serves as a Board or committee member for the Academy of American Orthopaedic Surgeons, Arthroscopy Association of North American, Eastern Orthopaedic Association and the American Orthopaedic Society for Sports Medicine. Dr. Kelly serves on the Editorial or Governing board of Orthopedics and Orthopedics today. Hao-Hua Wu, Max Liu and Grant Garcia MD have nothing to disclose.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

[licenses/by-nc/4.0/](http://creativecommons.org/licenses/by-nc/4.0/)

Manuscript source: Invited manuscript

Correspondence to: Dr. Hao-Hua Wu, Jordan Medical Education Center, 3400 Civic Center Blvd, 5th Floor, Philadelphia, PA 19104, United States. haohuawu@gmail.com
Telephone: +1-806-7905735
Fax: +1-215-3498312

Received: March 11, 2016

Peer-review started: March 12, 2016

First decision: May 19, 2016

Revised: July 12, 2016

Accepted: August 17, 2016

Article in press: August 18, 2016

Published online: November 18, 2016

Abstract

While most patients with an anterior cruciate ligament (ACL) injury indicate satisfaction with surgical intervention, a significant proportion still do not return to pre-injury level of function or sport. Psychiatric comorbidities, such as depression, have recently been associated with poor clinical outcomes after ACL reconstruction (ACLR). To date, no article has yet examined how depression affects ACLR outcomes and how potential screening and intervention for psychological distress may affect postoperative activity level. The purpose of this review is to delineate potential relationships between depression and ACLR outcome, discuss clinical implications and identify future directions for research.

Key words: Depression; Preoperative evaluation; Anxiety; Anterior cruciate ligament reconstruction; Patient reported outcome; Orthopedic surgery

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A difference exists between patients suffering

from psychiatric disease, such as depression, and those with psychological constructs, such as pain catastrophization, that hinder sport performance. The former may require clinical evaluation by a mental health professional. The latter may be dealt with through counseling and physical therapy. When assessing a patient with anterior cruciate ligament injury, it may be useful to screen for symptoms of hopelessness and anhedonia that have persisted for at least two weeks, two inquiries found on the Patient Health Questionnaire 2 (PHQ-2). Patients who respond positively to the PHQ-2 should be referred for further evaluation and counseled accordingly.

Wu HH, Liu M, Dines JS, Kelly JD, Garcia GH. Depression and psychiatric disease associated with outcomes after anterior cruciate ligament reconstruction. *World J Orthop* 2016; 7(11): 709-717 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/709.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.709>

INTRODUCTION

The anterior cruciate ligament (ACL) is the most commonly injured ligament of the knee^[1]. Although treatment with ACL reconstruction (ACLR) can restore stability and knee kinematics^[2], a significant proportion of ACLR patients still do not return to pre-injury level of activity or sport^[1,3-6]. In recreational and professional athletes, Ardern *et al.*^[1] found that as much as 40% do not return to pre-injury level of sport two years postoperatively. Investigating this discouraging result, recent literature has recognized an association between psychological factors and ACLR outcome^[2,7-25].

In the continuum of psychological factors, clinical depression has recently been suggested as one of the most debilitating^[26-29]. Garcia *et al.*^[26] found that preoperative depressive symptomatology is associated with significantly worse self-reported functional outcome at one year postoperatively for patients undergoing ACLR^[26]. In addition, as many as two out of every five ACLR candidates may exhibit significant depressive symptomatology preoperatively^[16,26], a fourfold higher rate than the national average^[30].

To date, no review article has examined the impact of psychiatric disease, such as depression, on ACLR outcome and clinical practice. Instead, most of the focus has been on other psychological factors, such as fear of reinjury, athletic identity, self-efficacy, and locus of control, which are not true clinical diagnoses^[2,10,14,15,20,22,25,28]. Although psychological impediments may interfere with ACLR rehabilitation, they rarely have implications outside of sport^[2,16,18]. In contrast, depression is associated with significant general comorbidities and is the major risk factor for suicide in ACLR patient age groups^[31-36]. While past ACLR literature has called for patients reporting depressive symptoms to seek care from a sports psychologist^[2], recent studies have advocated

for depression screening tools and referral to mental health professionals, where therapy and pharmacologic treatment may be necessary^[15,26].

The purpose of this review is to delineate potential associations between depression and ACLR outcome, discuss clinical implications and identify future directions for research.

DEPRESSION SYMPTOMATOLOGY AND ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

In the United States, the second-most likely cause of death for patients in the 15-34 age group is suicide^[31]. According to the American Psychiatric Association, major depressive disorder (MDD) is the most salient risk factor for suicide^[32,37] and is estimated to affect up to 10% of the adult United States population^[30]. Individuals can meet diagnostic criteria for MDD when they exhibit at least five out of nine depression symptoms, such as anhedonia or hopelessness, for a duration of at least two weeks without the influence of substances (Table 1). Depression accounts for \$43 billion in medical costs annually and by 2020 could be the second largest cause of disability^[38]. Given the prevalence and impact of depression, many primary care specialties recommend guidelines for screening, treatment and referral^[38].

Although the Academy of American Orthopaedic Surgeons (AAOS) and American Orthopaedic Society for Sports Medicine (AOSSM) do not have guidelines in place for when to screen orthopaedic patients for symptoms of depression, recent literature suggests that depression can significantly affect orthopaedic patients and outcomes^[15]. For instance, the incidence for depression can be as high as 45% in orthopaedic trauma patients^[39], 42% in ACLR patients^[26], and above national average level for patients undergoing joint replacement^[40] and rotator cuff repair^[41]. In addition, depression has been found to be a risk factor for poor functional outcome for orthopaedic procedures with lengthy rehabilitation periods, such as joint replacement and vertebral disc replacement^[40,42]. Common symptoms of depression, such as fatigue, psychomotor agitation, and inability to concentrate, may interfere with rehabilitation^[32], particularly if recovery takes at least one year^[2].

Given the patient demographic and length of rehabilitation, ACLR and its association with depression has drawn recent interest. It is known that 15-25 year-olds have the highest incidence of ACL injury, which make patients of this age group common ACLR candidates^[12]. However, this is the same age-group vulnerable to the sequelae of depression, as suicide remains the second most common cause of death^[37]. In addition, rehabilitation after ACLR has long been recognized as an important aspect to recovery and return to sport^[6]. Compliance with rehab, however, can be especially difficult for those afflicted with depression due to the

Table 1 Diagnostic criteria of major depressive disorder¹

DSM-V	Diagnostic Criteria
Major depressive disorder	<p>Patient reports at least five of nine of the following depressive symptoms most of the day or almost every day for at least two weeks:</p> <p>(1) Depressed mood that may be characterized by sadness, emptiness or hopelessness; (2) Markedly diminished interest or pleasure in all or almost all activities; (3) Significant unexpected weight loss; (4) Inability to sleep or oversleeping; (5) Psychomotor agitation or retardation; (6) Fatigue or loss of energy; (7) Feelings of worthlessness or inappropriate guilt; (8) Diminished ability to think, concentrate or make decisions; (9) Recurrent thoughts of death, suicidal ideation without a specific plan or a specific suicide attempt or specific plan for committing suicide</p> <p>Symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning</p> <p>The episode is not due to the effects of substance or to a medical condition</p> <p>The occurrence is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders</p> <p>There has never been a manic episode or a hypomanic episode</p>

¹Adapted from the DSM-V guidelines.

length and intensity of exercise^[6].

RECOVERY FROM ACLR: A LENGTHY REHAB PROCESS

A number of postoperative rehabilitation protocols exist for ACL reconstruction patients, and many are physically demanding; however, there is minimal consensus as to which programs are most effective^[43]. In general, programs can incorporate early weight bearing and motion, closed kinetic chain exercises, cryotherapy and exercises to enhance balance, proprioception, and core strength^[44-48]. These are implemented at various stages in a tiered fashion beginning with controlling inflammation and restoring gait which later progresses to normalizing range of motion, strength, and activity^[46,49]. Other components of a physical therapy regimen such as neuromuscular electrical stimulation (electrotherapy), gait training, hydrotherapy, stair climber, and slide board programs have also been found to be safe and beneficial to some^[45-48]. In contrast, there is little evidence to support the use of a knee brace, continuous passive motion, or creatine supplements to enhance recovery^[47,48].

While most protocols are similar in the activities that are prescribed, they vary greatly on the time frame in which increasing levels of activity are permitted. Traditional rehabilitation programs tend to be more conservative in the level of activity permitted at each phase of treatment and typically require approximately one year to complete^[50]. Recently, aggressive protocols have become popular and have reduced the length down to 6 mo before return to full active function^[48,50-52]. These more progressive regimes typically allow full range of motion at 10 wk and return to sports if strength is greater than 80% as early as 16 wk^[43,46-48,50,52]. The number of physical therapy sessions in these accelerated programs varies greatly but generally averages around 20 sessions, most of which occur in the first three months^[49,53]. Home based programs, which average around 4 sessions within the same timeframe, have been found to be equally effective for motivated patients^[47,53-57].

Regardless of the exact regimen followed, the road to recovery requires myriad hours of physical therapy to return to pre-injury level of activity. In addition, return to full, pre-injury state function does not always occur. For instance, Schenck *et al*^[54] found that patients returned to good function on average at 21.6 mo (range: 12-48). In a meta-analysis conducted by Arden *et al*^[6], only 63% of patients were able to return to their pre-injury sport; 44% returned to competition. The average time between surgery and the resumption of any type or level of sports was 7.3 (range 2-24) mo, and those that returned to competition required on average 36.7 mo postoperatively^[3].

The psychosocial impact of such a long recovery process can be particularly devastating. A lack of mobility may result in social isolation and lowered self-efficacy or a loss of self-worth as a result of not being able to perform pre-injury state functions^[15]. The latter is particularly applicable for collegiate or professional athletes who gain a strong sense of self-worth from their physical performance capabilities^[58]. For instance, collegiate athletes who sustained ACL injuries demonstrated seven times more depression relative to baseline and exhibited mood disturbances, anger, depression, and lowered self-esteem^[10,17,27,59]. Those who suffered career ending injuries reported much lower life satisfaction scores compared to their non-injured counterparts^[27]. Those that require knee stability as part of their occupation, such as military personnel and manual laborers, are also severely affected by the long recovery process. A study conducted by the Australian Army found that only 71% of personnel who underwent ACLR returned to active duty after 3 years^[60,61]. Particular emphasis must be placed on these patient populations to minimize psychosocial health deterioration during the rehabilitation process^[62].

THE MECHANISM OF DEPRESSION AND IMPLICATIONS FOR RECOVERY

Although it has been shown that depressed patients undergoing ACLR report lower self-reported outcome

Table 2 Systemic effects of clinical depression on immune system and hypothalamic-pituitary-adrenal axis

Target system	Effect
Immunologic system	Increased interleukin-1 Increased interleukin-6 Increased tumor necrosis factor- α
Musculoskeletal system	Decreased bone formation Increased bone resorption (likely 2/2 increased interleukin-1 and subsequent osteoclast activity)
Hypothalamic-pituitary-adrenal axis	Increased cortisol

scores, it is unclear why. Since no randomized controlled studies have been conducted, causation has yet to be determined. ACL injury alone may lead to depressed mood and depressed mood may lead to poor self-reported functional outcome. Adherence to rehabilitation protocol after ACL reconstruction has been shown to strongly correlate with surgical outcome^[18]. Thus, one possible explanation for compromised subjective outcomes in depressed patients is that those who experience greater symptoms of depression are less likely to adhere to the necessary rigorous ACL rehabilitation, leading to poorer clinical outcomes. Other literature propose fear of reinjury, pain catastrophizing and a lower internal Health Locus of Control - defined as the perception of one's ability to control life events - as other possible mechanisms^[63]. It is plausible that ACL patients who are depressed are more likely to have these aforementioned psychosocial impediments that can disrupt the recovery process. Indeed, successful recovery from surgical intervention has been suggested to require a dynamic biopsychosocial cycle consisting of a patient's affect, cognition and behavior^[22]. Thus, it is also possible that clinical depression is just one in a continuum of psychosocial and musculoskeletal factors that contribute to surgical outcome^[18,22,63].

In addition, it has been suggested that depression is a systemic disorder with increased inflammatory markers that contribute to worse medical outcome^[33,64,65] (Table 2). In addition to decreased serotonin levels, depressed patients have been found to have elevated levels of interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)- α , decreased cell-mediated immunity and increased cytokine response compared to non-depressed HIV and cardiovascular disease patients^[33,64,65]. These cytokines are particularly significant to musculoskeletal injury since IL-1 activates osteoclasts, thereby decreasing bone formation and density, while IL-6 and TNF- α are acute phase reactants that are implicated in fever and inflammation^[33]. While depression may certainly exacerbate psychological impediments to recovery, there may be an immunologic basis as well, a concept that warrants future investigation.

OTHER PSYCHIATRIC DISEASE AND ACLR

Other common psychiatric diseases, such as anxiety and

psychotic disorders, have not been studied with respect to recovery after ACLR, but have been implicated in orthopaedic disease. For instance, many studies have noted an elevated incidence of preoperative anxiety disorders in orthopaedic patients such as those with osteonecrosis of the femoral head^[66-68], which have led to worse patient reported outcomes for joint replacement patients^[69-72]. Others have noted that anxiety disorders, such as posttraumatic stress disorder have led to worse clinical outcome following lower extremity orthopedic surgery for patients^[73-76].

In addition, psychotic disorders such as schizophrenia and delirium have been implicated in worse postoperative outcome and leaving the hospital against medical advice^[77-80]. In orthopaedic patients, it has been suggested that patients with psychiatric disease may have increased hypothalamic-pituitary-adrenal (HPA) responses to the stress of surgery^[34]. As Kudoh *et al.*^[34] suggests, elevated cortisol may accelerate injury to vascular endothelial cells and promote the development of atherosclerosis or hypertension.

However, no studies have yet to look at anxiety and psychotic disorders and their association with ACLR outcome.

RECOMMENDATIONS FOR CLINICAL PRACTICE: EVALUATION OF ACLR CANDIDATE

Evaluation of ACL reconstruction candidates requires obtaining a pertinent history, performing a thorough physical exam, and utilizing diagnostic imaging. Classically, patients with ACL tears will complain of a "popping" sensation followed by acute swelling and a feeling that their knee is unstable. Other aspects of a clinical history to elicit include time and mechanism of injury, location of pain, and functional ability. On the physical exam, general evaluation for knee pain should be conducted which include inspection, palpation, and testing for mobility, strength, and stability. Specialized tests for ACL integrity include the Lachman, Pivot Shift, and Anterior Drawer^[81-83]. While all three should be performed, the Lachman has been shown to be the most useful^[83]. Sensitivity and specificity of the Lachman for ACL tears have been reported at 84% and 94%, respectively^[83]. Comparison with the contralateral knee is also important as many patients have increased laxity that may not be

Table 3 Patient Health Questionnaire 2¹

Over the past 2 wk, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
Litter interest or pleasure in doing things	0 ²	1 ²	2 ²	3 ²
Feeling down, depressed, or hopeless	0 ²	1 ²	2 ²	3 ²

¹Adapted from Arroll *et al.*^[86]; ²Sum points from both questions (range 0-6). A score of 3 or higher is considered positive and should be further evaluated by Patient Health Questionnaire-9.

Table 4 Diagnostic criteria for major depressive disorder utilizing SIGECAPS mnemonic¹

Sleep	Insomnia or hypersomnia nearly every day
Interest	Markedly diminished interest or pleasure in nearly all activities most of the time
Guilt	Excessive or inappropriate feelings of guilt or worthlessness most of the time
Energy	Loss of energy or fatigue most of the time
Concentration	Diminished ability to think or concentrate; indecisiveness most of the time
Appetite	Increase or decrease in appetite
Psychomotor	Observed psychomotor agitation/retardation
Suicide	Recurrent thoughts of death/suicidal ideation

¹Adapted from the Diagnostic and Statistical Manual of Mental Disorder, 4th ed.

pathologic. Lastly, MRI imaging may be used to assist with diagnosis^[83]. Together, the constellation of signs and symptoms can be used to determine whether the patient is a candidate for ACLR.

Recommendations for managing an ACLR patient with depression center on three domains: Stratifying risk, screening for early signs of mental health deterioration, and implementing effective interventions. Risk stratification involves identifying patients who may have poor postoperative rehabilitation outcomes as a result of their mental health state. This can be performed both preoperatively and postoperatively. While depression is not an absolute contraindication for surgery, if it is identified at the preoperatively, consideration can be made to delay surgery so that the patient can seek mental health services^[15]. Postoperatively, those who are considered high-risk should be monitored more closely. Emphasis should be placed on demographic groups that have been shown to be the most affected by ACL injury and the lengthy recovery process including athletes, military personnel, and manual laborers^[59-62,84]. Those who exhibit high levels of psychological stress or low levels of self-efficacy should also be placed in the high-risk category given literature suggesting a connection between these two factors and poor recovery from injury or surgery^[15,85].

Most importantly, many questionnaires exist for screening depression, including the Patient Health Questionnaire (PHQ), Center for Epidemiologic Studies Depression Scale (CESDS), and Geriatric Depression Scale (GDS)^[15,38,86]. Among the validated tests, perhaps the one that is most applicable to the ACLR population is the PHQ which, due to a concise format that can be applied rapidly in an orthopedic setting^[86] (Table 3). It involves a short, two question survey (PHQ-2) to screen

for depressed mood and anhedonia over the past 2 wk. Those that screen positive are then evaluated by the longer PHQ-9, a nine-question survey. The PHQ-2 may rule out, but not definitively diagnose, depression, but is as effective as longer screening instruments, such as the Beck Depression Inventory. The PHQ-2, for instance, has been found to be up to 97% sensitive in adults. In addition to the PHQ-2, SIGECAPS is also a popular mnemonic that can be easily used by orthopedic surgeons or physical therapists to quickly screen for different manifestations of depression^[33] (Table 4).

A number of interventions have been recommended for ACLR patients with depression, although it is important to note that none have been studied with respect to ACLR outcomes. Most suggest referral to a primary care or mental health provider with the application of pharmacotherapy if indicated^[2,15]. Existing psychiatric literature suggests that pharmacologic intervention can improve medical outcome, such as decreasing mortality in HIV and cardiovascular patients^[33,65]. In the orthopaedic literature, referral to a sports psychologist, pain desensitization therapy, cognitive behavioral pain management, goal setting, and positive self-talk courses, books, or audiotapes^[15,48]. Specific interventions include attending preoperative education classes or developing a peer support network with previous patients or athletes who have recovered from injury. Given the link between physical therapy adherence and outcomes, it may also be beneficial to increase the number of in-office sessions for ACLR patients with depressed symptomatology especially in the later stages of treatment where more home sessions are typically prescribed. Indeed, patients with or without MDD who adhere to the same in-office schedule report similar outcomes in the early phase of treatment^[26]. Conversely, home based programs with

minimal supervision have only been shown to be effective in motivated individuals with high self-efficacy^[47,53], which would not be recommended to potentially depressed ACLR patients. Establishing a treatment pathway for preoperatively depressed ACLR patients could help improve rehabilitation adherence and potentially functional outcomes.

RECOMMENDATIONS FOR FUTURE RESEARCH

Review of the literature leads to three recommendations for future research regarding ACLR patients and their association with psychiatric disease. First, it is clear while recent literature suggests an association exists between depression and ACLR outcome, more work is needed to elicit the significance of the chronology of the mood disturbance and its effects. For instance, do only patients with preoperative depression symptomatology perform worse or do the symptoms primarily manifest in the recovery phase? In addition, up to how long postoperatively do patients classified as having MDD report worse outcomes than non-MDD counterparts? Currently, there is no literature on outcomes past one-year follow-up; second, research examining the importance of intervention for ACLR patients with depression symptomatology is needed. While many studies encourage providers to be aware of depression symptomatology, there has yet to be evidence that intervention, whether through referral, behavioral therapy, or pharmacotherapy, can improve outcomes; lastly, future studies should also examine other common psychiatric disorders, such as general anxiety disorder and PTSD, since these have been implicated in poor outcome for patients undergoing other orthopaedic procedures.

CONCLUSION

Existing literature suggests that patients who sustain ACL injury may report higher rates the national average of depression symptomatology and that these symptoms may be associated with worse postoperative outcome. Providers should therefore consider screening ACLR candidates for depression, perhaps with the PHQ-2. Future research should strive to delineate the timing of depression in ACLR patients, the effect of interventions and whether other psychiatric diseases are associated with ACLR outcomes.

REFERENCES

- 1 **Ardern CL**, Taylor NF, Feller JA, Whitehead TS, Webster KE. Sports participation 2 years after anterior cruciate ligament reconstruction in athletes who had not returned to sport at 1 year: a prospective follow-up of physical function and psychological factors in 122 athletes. *Am J Sports Med* 2015; **43**: 848-856 [PMID: 25583757 DOI: 10.1177/0363546514563282]
- 2 **Christino MA**, Fantry AJ, Vopat BG. Psychological Aspects of Recovery Following Anterior Cruciate Ligament Reconstruction. *J Am Acad Orthop Surg* 2015; **23**: 501-509 [PMID: 26209145 DOI: 10.5435/JAAOS-D-14-00173]
- 3 **Ardern CL**, Taylor NF, Feller JA, Webster KE. Return-to-sport outcomes at 2 to 7 years after anterior cruciate ligament reconstruction surgery. *Am J Sports Med* 2012; **40**: 41-48 [PMID: 21946441 DOI: 10.1177/0363546511422999]
- 4 **Ardern CL**, Taylor NF, Feller JA, Webster KE. Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors. *Br J Sports Med* 2014; **48**: 1543-1552 [PMID: 25157180 DOI: 10.1136/bjsports-2013-093398]
- 5 **Ardern CL**, Webster KE, Taylor NF, Feller JA. Return to the preinjury level of competitive sport after anterior cruciate ligament reconstruction surgery: two-thirds of patients have not returned by 12 months after surgery. *Am J Sports Med* 2011; **39**: 538-543 [PMID: 21098818 DOI: 10.1177/0363546510384798]
- 6 **Ardern CL**, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med* 2011; **45**: 596-606 [PMID: 21398310 DOI: 10.1136/bjism.2010.076364]
- 7 **Ardern CL**, Taylor NF, Feller JA, Whitehead TS, Webster KE. Psychological responses matter in returning to preinjury level of sport after anterior cruciate ligament reconstruction surgery. *Am J Sports Med* 2013; **41**: 1549-1558 [PMID: 23733635 DOI: 10.1177/0363546513489284]
- 8 **Bien DP**, Dubuque TJ. Considerations for late stage acl rehabilitation and return to sport to limit re-injury risk and maximize athletic performance. *Int J Sports Phys Ther* 2015; **10**: 256-271 [PMID: 25883874]
- 9 **Brand E**, Nyland J. Patient outcomes following anterior cruciate ligament reconstruction: the influence of psychological factors. *Orthopedics* 2009; **32**: 335 [PMID: 19472959 DOI: 10.3928/01477447-20090502-01]
- 10 **Brewer BW**, Cornelius AE. Self-Protective Changes in Athletic Identity Following Anterior Cruciate Ligament Reconstruction. *Psychol Sport Exerc* 2010; **11**: 1-5 [PMID: 20161402 DOI: 10.1016/j.psychsport.2009.09.005]
- 11 **Brewer BW**, Cornelius AE, Sklar JH, Van Raalte JL, Tennen H, Armeli S, Corsetti JR, Brickner JC. Pain and negative mood during rehabilitation after anterior cruciate ligament reconstruction: a daily process analysis. *Scand J Med Sci Sports* 2007; **17**: 520-529 [PMID: 17076828]
- 12 **Brewer BW**, Cornelius AE, Van Raalte JL, Petitpas AJ, Sklar JH, Pohlman MH, Krushell RJ, Ditmar TD. Age-Related Differences in Predictors of Adherence to Rehabilitation After Anterior Cruciate Ligament Reconstruction. *J Athl Train* 2003; **38**: 158-162 [PMID: 12937528]
- 13 **Brewer BW**, Cornelius AE, Van Raalte JL, Tennen H, Armeli S. Predictors of adherence to home rehabilitation exercises following anterior cruciate ligament reconstruction. *Rehabil Psychol* 2013; **58**: 64-72 [PMID: 23438001 DOI: 10.1037/a0031297]
- 14 **Czuppon S**, Racette BA, Klein SE, Harris-Hayes M. Variables associated with return to sport following anterior cruciate ligament reconstruction: a systematic review. *Br J Sports Med* 2014; **48**: 356-364 [PMID: 24124040 DOI: 10.1136/bjsports-2012-091786]
- 15 **Flanigan DC**, Everhart JS, Glassman AH. Psychological Factors Affecting Rehabilitation and Outcomes Following Elective Orthopaedic Surgery. *J Am Acad Orthop Surg* 2015; **23**: 563-570 [PMID: 26195567 DOI: 10.5435/JAAOS-D-14-00225]
- 16 **Langford JL**, Webster KE, Feller JA. A prospective longitudinal study to assess psychological changes following anterior cruciate ligament reconstruction surgery. *Br J Sports Med* 2009; **43**: 377-381 [PMID: 19019910 DOI: 10.1136/bjism.2007.044818]
- 17 **Morrey MA**, Stuart MJ, Smith AM, Wiese-Bjornstal DM. A longitudinal examination of athletes' emotional and cognitive responses to anterior cruciate ligament injury. *Clin J Sport Med* 1999; **9**: 63-69 [PMID: 10442619 DOI: 10.1097/00042752-199904000-00004]

- 18 **te Wierike SC**, van der Sluis A, van den Akker-Scheek I, Elferink-Gemser MT, Visscher C. Psychosocial factors influencing the recovery of athletes with anterior cruciate ligament injury: a systematic review. *Scand J Med Sci Sports* 2013; **23**: 527-540 [PMID: 23121478]
- 19 **Everhart JS**, Best TM, Flanigan DC. Psychological predictors of anterior cruciate ligament reconstruction outcomes: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 752-762 [PMID: 24126701]
- 20 **Udry E**, Donald Shelbourne K, Gray T. Psychological Readiness for Anterior Cruciate Ligament Surgery: Describing and Comparing the Adolescent and Adult Experiences. *J Athl Train* 2003; **38**: 167-171 [PMID: 12937530]
- 21 **Thoméé P**, Währborg P, Börjesson M, Thoméé R, Eriksson BI, Karlsson J. A new instrument for measuring self-efficacy in patients with an anterior cruciate ligament injury. *Scand J Med Sci Sports* 2006; **16**: 181-187 [PMID: 16643196 DOI: 10.1111/j.1600-0838.2005.00472.x]
- 22 **Nyland J**, Cottrell B, Harreld K, Caborn DN. Self-reported outcomes after anterior cruciate ligament reconstruction: an internal health locus of control score comparison. *Arthroscopy* 2006; **22**: 1225-1232 [PMID: 17084301 DOI: 10.1016/j.arthro.2006.05.034]
- 23 **Thoméé P**, Währborg P, Börjesson M, Thoméé R, Eriksson BI, Karlsson J. Determinants of self-efficacy in the rehabilitation of patients with anterior cruciate ligament injury. *J Rehabil Med* 2007; **39**: 486-492 [PMID: 17624484 DOI: 10.2340/16501977-0079]
- 24 **Thoméé P**, Währborg P, Börjesson M, Thoméé R, Eriksson BI, Karlsson J. Self-efficacy of knee function as a pre-operative predictor of outcome 1 year after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 118-127 [PMID: 18034333 DOI: 10.1007/s00167-007-0433-6]
- 25 **Mendoza M**, Patel H, Bassett S. Influences of psychological factors and rehabilitation adherence on the outcome post anterior cruciate ligament injury/surgical reconstruction. *N Z J Physiother* 2007; **35**: 62-71. Available from: URL: <http://aut.researchgateway.ac.nz/handle/10292/1974>
- 26 **Garcia GH**, Wu HH, Park MJ, Tjoumakaris FP, Tucker BS, Kelly JD, Sennett BJ. Depression Symptomatology and Anterior Cruciate Ligament Injury: Incidence and Effect on Functional Outcome--A Prospective Cohort Study. *Am J Sports Med* 2016; **44**: 572-579 [PMID: 26628516 DOI: 10.1177/0363546515612466]
- 27 **Mainwaring LM**, Hutchison M, Bisschop SM, Comper P, Richards DW. Emotional response to sport concussion compared to ACL injury. *Brain Inj* 2010; **24**: 589-597 [PMID: 20235761 DOI: 10.3109/02699051003610508]
- 28 **Oztekin HH**, Boya H, Ozcan O, Zeren B, Pinar P. Pain and affective distress before and after ACL surgery: a comparison of amateur and professional male soccer players in the early postoperative period. *Knee* 2008; **15**: 368-372 [PMID: 18635361 DOI: 10.1016/j.knee.2008.05.007]
- 29 **Tripp DA**, Stanish WD, Reardon G, Coady C, Sullivan MJ. Comparing Postoperative Pain Experiences of the Adolescent and Adult Athlete After Anterior Cruciate Ligament Surgery. *J Athl Train* 2003; **38**: 154-157 [PMID: 12937527]
- 30 Current depression among adults---United States, 2006 and 2008. *MMWR Morb Mortal Wkly Rep* 2010; **59**: 1229-1235 [PMID: 20881934]
- 31 **CDC**. Ten Leading Causes of Death and Injury. [accessed 2016 Jan 30]. Available from: URL: <http://www.cdc.gov/injury/wisqars/leadingcauses.html>
- 32 **APA**. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Association, 2013
- 33 **Evans DL**, Charney DS, Lewis L, Golden RN, Gorman JM, Krishnan KR, Nemeroff CB, Bremner JD, Carney RM, Coyne JC, Delong MR, Frasure-Smith N, Glassman AH, Gold PW, Grant I, Gwyther L, Ironson G, Johnson RL, Kanner AM, Katon WJ, Kaufmann PG, Keefe FJ, Ketter T, Laughren TP, Leserman J, Lyketsos CG, McDonald WM, McEwen BS, Miller AH, Musselman D, O'Connor C, Petitto JM, Pollock BG, Robinson RG, Roose SP, Rowland J, Sheline Y, Sheps DS, Simon G, Spiegel D, Stunkard A, Sunderland T, Tibbitts P, Valvo WJ. Mood disorders in the medically ill: scientific review and recommendations. *Biol Psychiatry* 2005; **58**: 175-189 [PMID: 16084838 DOI: 10.1016/j.biopsych.2005.05.001]
- 34 **Kudoh A**, Kudo T, Ishihara H, Matsuki A. Depressed pituitary-adrenal response to surgical stress in chronic schizophrenic patients. *Neuropsychobiology* 1997; **36**: 112-116 [PMID: 9313243 DOI: 10.1159/000119372]
- 35 **Kudoh A**, Takahira Y, Katagai H, Takazawa T. Schizophrenic patients who develop postoperative confusion have an increased norepinephrine and cortisol response to surgery. *Neuropsychobiology* 2002; **46**: 7-12 [PMID: 12207140 DOI: 10.1159/000063569]
- 36 **Griffin LY**, Agel J, Albohm MJ, Arendt EA, Dick RW, Garrett WE, Garrick JG, Hewett TE, Huston L, Ireland ML, Johnson RJ, Kibler WB, Lephart S, Lewis JL, Lindenfeld TN, Mandelbaum BR, Marchak P, Teitz CC, Wojtyk EM. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J Am Acad Orthop Surg* 2000; **8**: 141-150 [PMID: 10874221 DOI: 10.5435/00124635-200005000-00001]
- 37 **Linkowski P**, de Maertelaer V, Mendlewicz J. Suicidal behaviour in major depressive illness. *Acta Psychiatr Scand* 1985; **72**: 233-238 [PMID: 4072720 DOI: 10.1111/j.1600-0447.1985.tb02600.x]
- 38 **Maurer DM**. Screening for depression. *Am Fam Physician* 2012; **85**: 139-144 [PMID: 22335214]
- 39 **Crichlow RJ**, Andres PL, Morrison SM, Haley SM, Vrahas MS. Depression in orthopaedic trauma patients. Prevalence and severity. *J Bone Joint Surg Am* 2006; **88**: 1927-1933 [PMID: 16951107 DOI: 10.2106/JBJS.D.02604]
- 40 **Browne JA**, Sandberg BF, D'Apuzzo MR, Novicoff WM. Depression is associated with early postoperative outcomes following total joint arthroplasty: a nationwide database study. *J Arthroplasty* 2014; **29**: 481-483 [PMID: 24090662 DOI: 10.1016/j.arth.2013.08.025]
- 41 **Cho CH**, Seo HJ, Bae KC, Lee KJ, Hwang I, Warner JJ. The impact of depression and anxiety on self-assessed pain, disability, and quality of life in patients scheduled for rotator cuff repair. *J Shoulder Elbow Surg* 2013; **22**: 1160-1166 [PMID: 23594716 DOI: 10.1016/j.jse.2013.02.006]
- 42 **Zieger M**, Schwarz R, König HH, Härter M, Riedel-Heller SG. Depression and anxiety in patients undergoing herniated disc surgery: relevant but underresearched - a systematic review. *Cent Eur Neurosurg* 2010; **71**: 26-34 [PMID: 20094980 DOI: 10.1055/s-0029-1225325]
- 43 **Delay BS**, Smolinski RJ, Wind WM, Bowman DS. Current practices and opinions in ACL reconstruction and rehabilitation: results of a survey of the American Orthopaedic Society for Sports Medicine. *Am J Knee Surg* 2001; **14**: 85-91 [PMID: 11401175]
- 44 **Gordon MD**, Steiner ME. Anterior cruciate ligament injuries. In: *Orthopaedic Knowledge Update Sports Medicine III*, Garrick JG. (Ed). 2004: 169
- 45 **Risberg MA**, Holm I, Myklebust G, Engebretsen L. Neuromuscular training versus strength training during first 6 months after anterior cruciate ligament reconstruction: a randomized clinical trial. *Phys Ther* 2007; **87**: 737-750 [PMID: 17442840 DOI: 10.2522/ptj.20060041]
- 46 **van Grinsven S**, van Cingel RE, Holla CJ, van Loon CJ. Evidence-based rehabilitation following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2010; **18**: 1128-1144 [PMID: 20069277 DOI: 10.1007/s00167-009-1027-2]
- 47 **Wright RW**, Preston E, Fleming BC, Amendola A, Andrich JT, Bergfeld JA, Dunn WR, Kaeding C, Kuhn JE, Marx RG, McCarty EC, Parker RC, Spindler KP, Wolcott M, Wolf BR, Williams GN. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part I: continuous passive motion, early weight bearing, postoperative bracing, and home-based rehabilitation. *J Knee Surg* 2008; **21**: 217-224 [PMID: 18686484 DOI: 10.1055/s-0030-1247822]
- 48 **Wright RW**, Preston E, Fleming BC, Amendola A, Andrich JT, Bergfeld JA, Dunn WR, Kaeding C, Kuhn JE, Marx RG, McCarty EC, Parker RC, Spindler KP, Wolcott M, Wolf BR, Williams GN. A systematic review of anterior cruciate ligament reconstruction

- rehabilitation: part II: open versus closed kinetic chain exercises, neuromuscular electrical stimulation, accelerated rehabilitation, and miscellaneous topics. *J Knee Surg* 2008; **21**: 225-234 [PMID: 18686485 DOI: 10.1055/s-0030-124782]
- 49 **De Carlo MS**, Sell KE. The effects of the number and frequency of physical therapy treatments on selected outcomes of treatment in patients with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 1997; **26**: 332-339 [PMID: 9402570 DOI: 10.2519/jospt.1997.26.6.332]
- 50 **Decarlo MS**, Shelbourne KD, McCarroll JR, Rettig AC. Traditional versus Accelerated Rehabilitation following ACL Reconstruction: A One-Year Follow-Up. *J Orthop Sports Phys Ther* 1992; **15**: 309-316 [PMID: 18781004 DOI: 10.2519/jospt.1992.15.6.309]
- 51 **Shelbourne KD**, Klootwyk TE, Decarlo MS. Update on accelerated rehabilitation after anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 1992; **15**: 303-308 [PMID: 18781000 DOI: 10.2519/jospt.1992.15.6.256]
- 52 **Grant JA**. Updating Recommendations for Rehabilitation after ACL Reconstruction: a Review. *Clin J Sport Med* 2013; **23**: 501-502 [PMID: 24169301 DOI: 10.1097/JSM.0000000000000044]
- 53 **Grant JA**, Mohtadi NG, Maitland ME, Zernicke RF. Comparison of home versus physical therapy-supervised rehabilitation programs after anterior cruciate ligament reconstruction: a randomized clinical trial. *Am J Sports Med* 2005; **33**: 1288-1297 [PMID: 16002493 DOI: 10.1177/0363546504273051]
- 54 **Schenck RC**, Blaschak MJ, Lance ED, Turturro TC, Holmes CF. A prospective outcome study of rehabilitation programs and anterior cruciate ligament reconstruction. *Arthroscopy* 1997; **13**: 285-290 [PMID: 9195022 DOI: 10.1016/S0749-8063(97)90022-0]
- 55 **Manal TJ**, Snyder-Mackler L. Practice guidelines for anterior cruciate ligament rehabilitation: A criterion-based rehabilitation progression. *Oper Tech Orthop* 1996; **6**: 190-196 [DOI: 10.1016/S1048-6666(96)80019-X]
- 56 **Adams D**, Logerstedt DS, Hunter-Giordano A, Axe MJ, Snyder-Mackler L. Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression. *J Orthop Sports Phys Ther* 2012; **42**: 601-614 [PMID: 22402434 DOI: 10.2519/jospt.2012.3871]
- 57 **Pereira M**, Vieira Nde S, Brandão Eda R, Ruaro JA, Grignet RJ, Fréz AR. Physiotherapy after reconstruction of anterior cruciate ligament. *Acta Ortop Bras* 2012; **20**: 372-375 [PMID: 24453634 DOI: 10.1590/S1413-78522012000600011]
- 58 **Brewer BW**, Van Raalte JL, Linder DE. Athletic identity: Hercules' muscles or Achilles heel? *Int J Sport Psychol* 1993; **24**: 237-254
- 59 **Smith AM**, Scott SG, Wiese DM. The psychological effects of sports injuries. Coping. *Sports Med* 1990; **9**: 352-369 [PMID: 2192425 DOI: 10.2165/00007256-199009060-00004]
- 60 **Weinrauch PC**, Sharwood P. Employment in the Australian Army after anterior cruciate ligament reconstruction - a pilot study of 3 year postoperative outcomes. *Austr Mil Med Ass J* 2006; **15**: 15-17. Available from: URL: http://jmvh.org/wp-content/uploads/2014/03/small_amm_v15_1.pdf
- 61 **Newcomer RR**, Perna FM. Features of Posttraumatic Distress Among Adolescent Athletes. *J Athl Train* 2003; **38**: 163-166 [PMID: 12937529]
- 62 **Tripp DA**, Stanish W, Ebel-Lam A, Birchard LJ. Fear of reinjury, negative affect, and catastrophizing predicting return to sport in recreational athletes with anterior cruciate ligament injuries at 1 year postsurgery. *Rehabil Psychol* 2011; **52**: 74-81 [DOI: 10.1037/0090-5550.52.1.74]
- 63 **Chmielewski TL**, Zeppieri G, Lentz TA, Tillman SM, Moser MW, Indelicato PA, George SZ. Longitudinal changes in psychosocial factors and their association with knee pain and function after anterior cruciate ligament reconstruction. *Phys Ther* 2011; **91**: 1355-1366 [PMID: 21700761 DOI: 10.2522/ptj.20100277]
- 64 **Marini S**, Vellante F, Matarazzo I, De Berardis D, Serroni N, Gianfelice D, Olivieri L, Di Renzo F, Di Marco A, Fornaro M, Orsolini L, Valchera A, Iasevoli F, Mazza M, Perna G, Martinotti G, Di Giannantonio M. Inflammatory markers and suicidal attempts in depressed patients: A review. *Int J Immunopathol Pharmacol* 2016 Jan 4; Epub ahead of print [PMID: 26729403 DOI: 10.1177/0394632015623793]
- 65 **Black C**, Miller BJ. Meta-Analysis of Cytokines and Chemokines in Suicidality: Distinguishing Suicidal Versus Nonsuicidal Patients. *Biol Psychiatry* 2015; **78**: 28-37 [PMID: 25541493 DOI: 10.1016/j.biopsych.2014.10.014]
- 66 **Chen SB**, Hu H, Gao YS, He HY, Jin DX, Zhang CQ. Prevalence of clinical anxiety, clinical depression and associated risk factors in chinese young and middle-aged patients with osteonecrosis of the femoral head. *PLoS One* 2015; **10**: e0120234 [PMID: 25789850 DOI: 10.1371/journal.pone.0120234]
- 67 **de Moraes VY**, Jorge MR, Faloppa F, Belloti JC. Anxiety and depression in Brazilian orthopaedics inpatients: a cross sectional study with a clinical sample comparison. *J Clin Psychol Med Settings* 2010; **17**: 31-37 [PMID: 20111986 DOI: 10.1007/s10880-009-9184-5]
- 68 **Demir B**, Gürsu S, Yildirim T, Er T. Evaluation of anxiety levels in patients with chronic orthopedic diseases. *Acta Orthop Traumatol Turc* 2012; **46**: 420-424 [PMID: 23428765 DOI: 10.3944/AOTT.2012.2756]
- 69 **Bilberg R**, Nørgaard B, Overgaard S, Roessler KK. Patient anxiety and concern as predictors for the perceived quality of treatment and patient reported outcome (PRO) in orthopaedic surgery. *BMC Health Serv Res* 2012; **12**: 244 [PMID: 22873940 DOI: 10.1186/1472-6963-12-244]
- 70 **Brownlow HC**, Benjamin S, Andrew JG, Kay P. Disability and mental health of patients waiting for total hip replacement. *Ann R Coll Surg Engl* 2001; **83**: 128-133 [PMID: 11320923]
- 71 **Goebel S**, Baumann B, Steinert A, Reppenhagen S, Faller H. [Elevated postoperative pain levels following orthopedic surgery. Depression as a strong predictor]. *Schmerz* 2010; **24**: 54-61 [PMID: 20143100 DOI: 10.1007/s00482-009-0883-5]
- 72 **Gouttebauge V**, Backx FJ, Aoki H, Kerkhoffs GM. Symptoms of Common Mental Disorders in Professional Football (Soccer) Across Five European Countries. *J Sports Sci Med* 2015; **14**: 811-818 [PMID: 26664278]
- 73 **Aaron DL**, Fadale PD, Harrington CJ, Born CT. Posttraumatic stress disorders in civilian orthopaedics. *J Am Acad Orthop Surg* 2011; **19**: 245-250 [PMID: 21536623 DOI: 10.5435/00124635-201105000-00001]
- 74 **Guerini F**, Morghen S, Lucchi E, Bellelli G, Trabucchi M. Depressive symptoms and one year mortality among elderly patients discharged from a rehabilitation ward after orthopaedic surgery of the lower limbs. *Behav Neurol* 2010; **23**: 117-121 [PMID: 21098965 DOI: 10.1155/2010/365341]
- 75 **Schwarz S**, Mangels M, Sohr G, Holme M, Worringen U, Rief W. [Patients with versus without psychological disorders in orthopedic rehabilitation]. *Schmerz* 2008; **22**: 67-74 [PMID: 18084781 DOI: 10.1007/s00482-007-0603-y]
- 76 **Yildiz C**, Uzun O, Sinici E, Ateşalp AS, Özşahin A, Başbozkurt M. [Psychiatric symptoms in patients treated with an Ilizarov external fixator]. *Acta Orthop Traumatol Turc* 2005; **39**: 59-63 [PMID: 15805756]
- 77 **Menendez ME**, van Dijk CN, Ring D. Who leaves the hospital against medical advice in the orthopaedic setting? *Clin Orthop Relat Res* 2015; **473**: 1140-1149 [PMID: 25187333 DOI: 10.1007/s11999-014-3924-z]
- 78 **Liang CK**, Chu CL, Chou MY, Lin YT, Lu T, Hsu CJ, Chen LK. Interrelationship of postoperative delirium and cognitive impairment and their impact on the functional status in older patients undergoing orthopaedic surgery: a prospective cohort study. *PLoS One* 2014; **9**: e110339 [PMID: 25402484 DOI: 10.1371/journal.pone.0110339]
- 79 **Fineberg SJ**, Nandyala SV, Marquez-Lara A, Oglesby M, Patel AA, Singh K. Incidence and risk factors for postoperative delirium after lumbar spine surgery. *Spine (Phila Pa 1976)* 2013; **38**: 1790-1796 [PMID: 23797502 DOI: 10.1097/BRS.0b013e3182a0d507]
- 80 **Buller LT**, Best MJ, Klika AK, Barsoum WK. The influence of psychiatric comorbidity on perioperative outcomes following primary total hip and knee arthroplasty; a 17-year analysis of the

- National Hospital Discharge Survey database. *J Arthroplasty* 2015; **30**: 165-170 [PMID: 25267536 DOI: 10.1016/j.arth.2014.08.034]
- 81 **Ostrowski JA.** Accuracy of 3 diagnostic tests for anterior cruciate ligament tears. *J Athl Train* 2006; **41**: 120-121 [PMID: 16619105]
- 82 **Solomon DH,** Simel DL, Bates DW, Katz JN, Schaffer JL. The rational clinical examination. Does this patient have a torn meniscus or ligament of the knee? Value of the physical examination. *JAMA* 2001; **286**: 1610-1620 [PMID: 11585485 DOI: 10.1001/jama.286.13.1610]
- 83 **Benjaminse A,** Gokeler A, van der Schans CP. Clinical diagnosis of an anterior cruciate ligament rupture: a meta-analysis. *J Orthop Sports Phys Ther* 2006; **36**: 267-288 [PMID: 16715828 DOI: 10.2519/jospt.2006.2011]
- 84 **Wexler G,** Bach BR, Bush-Joseph CA, Smink D, Ferrari JD, Bojchuk J. Outcomes of anterior cruciate ligament reconstruction in patients with Workers' Compensation claims. *Arthroscopy* 2000; **16**: 49-58 [PMID: 10627345 DOI: 10.1016/S0749-8063(00)90127-0]
- 85 **Cohen S,** Wills TA. Stress, social support, and the buffering hypothesis. *Psychol Bull* 1985; **98**: 310-357 [PMID: 3901065 DOI: 10.1037/0033-2909.98.2.310]
- 86 **Arroll B,** Goodyear-Smith F, Crengle S, Gunn J, Kerse N, Fishman T, Falloon K, Hatcher S. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *Ann Fam Med* 2010; **8**: 348-353 [PMID: 20644190 DOI: 10.1370/afm.1139]

P- Reviewer: Papachristou GC, Seijas R **S- Editor:** Kong JX
L- Editor: A **E- Editor:** Lu YJ



Management of syndesmotic injuries: What is the evidence?

Marc Schnetzke, Sven Y Vetter, Nils Beisemann, Benedict Swartman, Paul A Grützner, Jochen Franke

Marc Schnetzke, Sven Y Vetter, Nils Beisemann, Benedict Swartman, Paul A Grützner, Jochen Franke, Department for Trauma and Orthopaedic Surgery, MINTOS - Medical Imaging and Navigation in Trauma and Orthopaedic Surgery, BG Trauma Center Ludwigshafen at Heidelberg University Hospital, 67071 Ludwigshafen am Rhein, Germany

Author contributions: All authors contributed to this manuscript.

Conflict-of-interest statement: The following authors declared potential conflicts of interest: The MINTOS research group had grants/grants pending from Siemens (Erlangen, Germany); Jochen Franke, MD, is a paid lecturer for Siemens; Paul A Grützner, MD, is a paid lecturer for Siemens.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Jochen Franke, MD, Department for Trauma and Orthopaedic Surgery, MINTOS - Medical Imaging and Navigation in Trauma and Orthopaedic Surgery, BG Trauma Center Ludwigshafen at Heidelberg University Hospital, Ludwig-Guttman-Strasse 13, 67071 Ludwigshafen am Rhein, Germany. jochen.franke@bgu-ludwigshafen.de
Telephone: +49-621-68102290
Fax: +49-621-68102285

Received: May 18, 2016

Peer-review started: May 19, 2016

First decision: July 5, 2016

Revised: August 26, 2016

Accepted: September 7, 2016

Article in press: September 8, 2016

Published online: November 18, 2016

Abstract

Ankle fractures are accompanied by a syndesmotic injury in about 10% of operatively treated ankle fractures. Usually, the total rupture of the syndesmotic ligaments with an external rotation force is associated with a Weber type B or C fracture or a Maisonneuve fracture. The clinical assessment should consist of a comprehensive history including mechanism of injury followed by a specific physical examination. Radiographs, and if in doubt magnetic resonance imaging, are needed to ascertain the syndesmotic injury. In the case of operative treatment the method of fixation, the height and number of screws and the need for hardware removal are still under discussion. Furthermore, intraoperative assessment of the accuracy of reduction of the fibula in the incisura using fluoroscopy is difficult. A possible solution might be the assessment with intraoperative three-dimensional imaging. The aim of this article is to provide a current concepts review of the clinical presentation, diagnosis and treatment of syndesmotic injuries.

Key words: Ankle sprain; Syndesmotic injury; Syndesmotic screw; Ankle; TightRope; Three-dimensional

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The aim of this article is to provide a current concepts review of the clinical presentation, diagnosis and management of syndesmotic lesions. Even if syndesmotic injuries are common, the appropriate management is still under discussion. Current treatment options are discussed and future directions are provided.

Schnetzke M, Vetter SY, Beisemann N, Swartman B, Grützner PA, Franke J. Management of syndesmotic injuries: What is the evidence? *World J Orthop* 2016; 7(11): 718-725 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/718.htm>

DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.718>

INTRODUCTION

Ankle fractures are accompanied by a syndesmotom injury in about 10% of operatively treated ankle fractures^[1-3]. Numerous mechanisms can lead to disruption of the syndesmotom complex, and the most accepted mechanism of injury is external rotation, hyperdorsiflexion and talar eversion^[4-6]. This leads to sequentially tearing the anterior inferior tibiofibular ligament and the deltoid complex or causing a malleolar fracture, the interosseous ligament and finally the posterior inferior tibiofibular ligament^[7-9]. In most cases, a total lesion of the syndesmotom ligaments is associated with a distal fibular fracture type Weber B or C or a proximal fibular fracture (Maisonneuve injury)^[10,11].

CLINICAL AND RADIOLOGICAL EVALUATION

Local swelling and tenderness are suspicious for a syndesmotom injury^[12]. There are several tests available such as the external rotation test, heel thump test, dorsiflexion compression test or the squeeze test to evaluate the integrity of the syndesmotom^[6]. However, in the presence of pain or swelling these tests are of limited use^[13]. Clinical tests for syndesmotom lesions have a low predictive value to verify a syndesmotom injury. Several authors could show that the external rotation test might be the most sensitive test with the lowest false-positive rate^[6,14].

Intraoperatively, the integrity of the syndesmotom can be checked by the external rotation test or the bone hook test, which is supposed to be more reliable (Figure 1). However, these tests are also limited by a poor inter-observer reliability, which further highlights the importance of both clinical examination and imaging to diagnose an injury of the syndesmotom^[13-15].

RADIOGRAPHS

Standard radiographic examination of the ankle should consist of at least two views: Lateral view and mortise view (Figures 2 and 3). The anterior-posterior (AP) view of the ankle can be obtained as a third view, but it does not provide any additional information regarding the reduction of the mortise. In case of suspicion of a proximal fibular fracture or an injury of the syndesmotom in the clinical examination or on plain radiographs of the ankle, standard radiographs of the whole lower leg should be obtained to exclude proximal fractures/ Maisonneuve injury (Figure 4)^[6].

If an ankle fracture is present, the fracture pattern is most commonly described using the AO comprehensive classification system^[16,17]. The plain radiographs should also be carefully checked for avulsion fractures of the

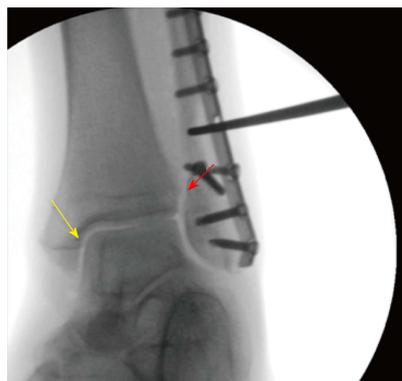


Figure 1 Intra-operative assessment of the syndesmotom integrity in a Weber B fracture with the hook test under fluoroscopy (Mortise view). In this case, the tibiofibular clear space (red arrow) and the medial clear space (yellow arrow) do not open indicating that the syndesmotom ligaments are intact.

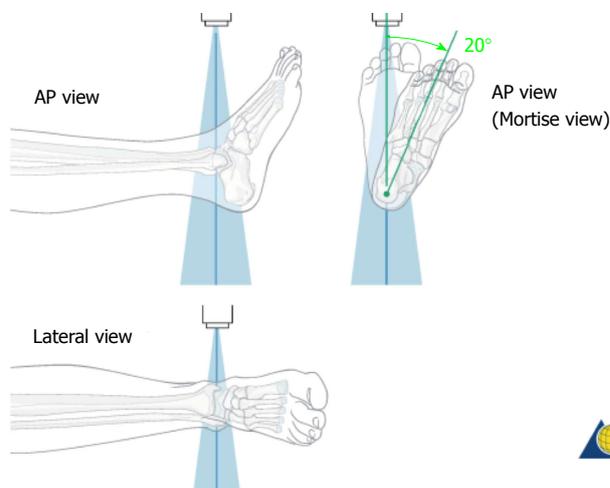


Figure 2 Illustration of the plain radiographs of the ankle (Copyright by AO Foundation, Switzerland). AP: Anterior-posterior.



Figure 3 Examples for radiographs of the ankle: Mortise view (A) and lateral view (B).

anterior part of the syndesmotom, the so-called Tubercule de Chaput or Wagstaffe le Fort fragment and the posterior malleolus (Volkman fragment) (Figure 5)^[18,19].

If the mechanism of injury and the clinical examination are suspicious for a syndesmotom injury, the

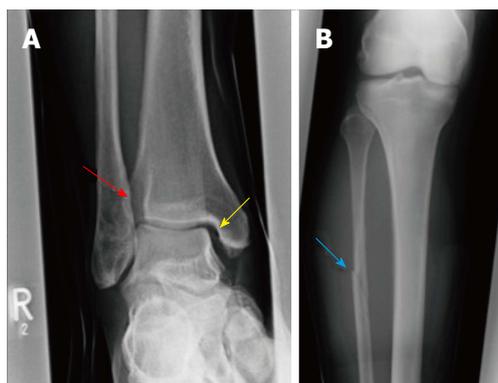


Figure 4 The increased tibiofibular clear space (red arrow) and medial clear space (yellow arrow) are highly suspicious for a syndesmotic lesion (A) and the radiograph of the proximal part of the lower leg is showing a Maisonneuve injury (blue arrow) (B).

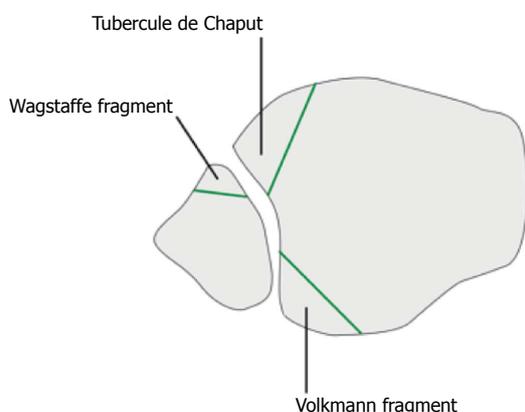


Figure 5 Schematic illustration of the avulsion fractures of the anterior part of the syndesmosis (Tubercle de Chaput, Wagstaffe fragment) and posterior Volkmann fragment (Copyright by AO Foundation, Switzerland).

plain radiography should be examined for: (1) the tibiofibular clear space; (2) the tibiofibular overlap; and (3) the increased medial clear space (Figure 4). These measurements are helpful to detect the presence of syndesmotic injuries^[19].

As a limitation, it should be mentioned that the measurements for the assessment of the syndesmosis on radiographs are based on cadaveric studies, and that the measurements are influenced by the quality of the radiographs. Recently, Hermans *et al*^[20] investigated a study to compare magnetic resonance imaging (MRI) findings with plain radiographs in syndesmotic injuries. The authors found that the tibiofibular overlap and the tibiofibular clear space did not correlate with a syndesmotic injury seen on MRI. Therefore, further imaging with MRI scan is recommended, if there is any suspicion of a syndesmotic lesion. The sensitivity and specificity of MRI scans for the evaluation of the syndesmotic complex is up to 100%, and the integrity of the syndesmosis can be optimally visualized on MRI axial views (Figure 6)^[21,22].

In addition to plain radiographs, manual or the gravity external rotation stress radiographs can be applied to the injured ankle to evaluate the integrity

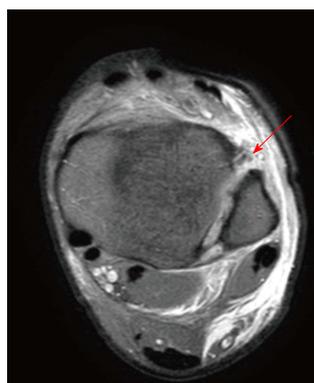


Figure 6 Axial plane of magnetic resonance imaging showing a full thickness tear of the anterior part of the syndesmosis (red arrow).

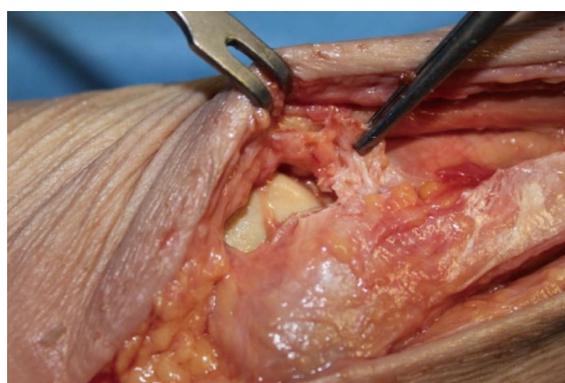


Figure 7 Intraoperative visualization of the anterior part of the syndesmosis; in this patient the anterior part of the syndesmosis is completely disrupted (hold with the pincers).

of the deltoid ligament^[23]. The amount of medial clear space widening of > 5 mm is highly suspicious for a rupture of the deep deltoid ligament. As a limitation of the manual stress test it should be mentioned that the amount of applied force necessary when performing an external rotation stress radiograph is not well defined and mainly determined by the patient's pain level^[23].

In the presence of fractures, clinical or radiological examination of the syndesmotic integrity is not necessary, as this can be done intraoperatively^[6]. Lui *et al*^[24] could show that arthroscopy can detect syndesmotic injuries more reliable than intraoperative stress radiographs. However, arthroscopy of the ankle joint is technically demanding and therefore, it is not used routinely. Normally, the integrity of the syndesmosis is checked by the hook test following fixation of ankle fractures (Figure 1). Alternatively, especially in unclear cases with fracture type Weber B, the integrity of the syndesmosis can be verified by intraoperative visualization and by intraoperative testing of the stability (Figure 7).

MANAGEMENT OF ISOLATED SYNDESMOTIC INJURIES

Syndesmotic injuries without an associated fracture

occur much less frequently compared to fracture associated syndesmotic lesions^[6,25]. However, if an isolated syndesmotic injury is missed, it is prone to deteriorated clinical outcome with pain and instability. The management of isolated syndesmotic injuries is still under discussion. In simple syndesmotic sprains without diastasis of the syndesmotic region most authors prefer non-operative management with a non-weight bearing cast and report good functional long-term results^[26]. In contrast, a displaced and widened mortise needs operative fixation of the syndesmosis^[26,27].

Non-surgical management

Non-surgical management includes plaster immobilization for 2-6 wk with a non weight-bearing cast^[26]. There are only few literature data available reporting on clinical results after conservative treatment of isolated syndesmotic injuries. Recently, a comprehensive review with isolated syndesmotic injuries has been published^[25]. The period of plaster immobilization varies between 2 and 6 wk indicating that there is no consensus. From our experience, plaster immobilization should be performed for at least 6 wk to prevent chronic instability and recurrent injuries.

The reported complication rates after non-surgical management of isolated syndesmotic injuries were high (up to 68%)^[28-30]. The most common complications recorded in the studies were stiffness, pain with activity, heterotopic ossification and residual painful instability.

Surgical management

Reports about operatively treated isolated syndesmotic injuries are rare. Taylor *et al*^[31] published the results of six patients with isolated syndesmotic injuries that were treated operatively with a 4.5-mm stainless steel cortical screw. The mean time from injury to treatment was 3 d and all the patients were treated within 7 d. Average time to return to sports was 40.7 d (32-48 d) in all patients. The assessment of the clinical outcome showed good to excellent results in all patients.

MANAGEMENT OF ANKLE FRACTURES WITH SYNDESMOTIC INJURIES

In the treatment of ankle fractures with an associated syndesmotic lesion the primary goal is to restore ankle stability and to maintain correct alignment of tibia and fibula to allow sufficient healing of the syndesmotic ligaments^[32]. In the case of surgical stabilization, the method of fixation is still under discussion^[6]. Beside the use of syndesmotic screws, which is the most widespread method, suturing of the syndesmosis, syndesmosis hooks, bioabsorbable screws, Endo Buttons (Smith and Nephew Endoscopy, Andover, Massachusetts), and the TightRope device (Arthrex, Naples, Florida), which in particular became popular in the last decade, are also used for syndesmotic fixation^[6].

Stabilization of the ankle mortise is generally recom-

mended, when the fracture pattern, intraoperative assessment with a hook or the direct visualization demonstrates a syndesmotic diastasis. A consensus for the appropriate size of the syndesmosis screw has not been reached yet. Most authors prefer either 3.5 or 4.5 mm cortical screws. In Europe most surgeons use one single 3.5-mm tricortical diastasis screw for stabilization of the syndesmosis in Weber B or C fractures. The preferred height is at 2.1 to 4 cm above the ankle joint line. Two syndesmotic screws are commonly used in Maisonneuve fractures^[33]. In biomechanical studies, 3.5 and 4.5 mm cortical screws showed comparable biomechanical characteristics^[34]. In cadaveric studies the influence of the numbers of syndesmotic screws has been investigated^[35]. There is evidence that two screws provide a better construct biomechanically compared to one diastasis screw alone.

The placement height of the syndesmotic screw and the number of cortices engaged with the diastasis screws are also the topic of an ongoing discussion. Beumer *et al*^[35] could show that there is no difference in clinical outcome comparing the engagement of three vs four cortices. Most authors agree that diastasis screws should be placed 2 to 3 cm proximal to the tibial plafond. Interestingly, the placement of diastasis screws at 2, 3 and 5 cm proximal to the ankle joint seems to have no influence on functional outcome^[36].

Despite the invention of novel devices such as the Tightrope or bioabsorbable screws for restoration and maintenance of the congruent syndesmosis following syndesmotic injury, the metallic syndesmotic screw is still considered to be the gold standard^[37]. A possible disadvantage of the syndesmotic screw is the need for implant removal. In general, the syndesmosis takes 8 to 12 wk to heal, and afterwards removal of the hardware is recommended by most authors^[38]. However, the hardware removal is accompanied by high complication rates such as wound infection, re-occurrence of screw breakage and diastasis during removal^[39]. Alternatively, the syndesmotic screw can be left *in situ*. Schepers published a review with 472 patients included with retained syndesmotic screws. Eighty patients had loose diastasis or broken screws^[40]. Despite this, there were no significant differences in clinical outcome between retained or removed screws.

Another alternative fixation device are bioabsorbable screws. Bioabsorbable screws can be used instead of syndesmotic screws for stabilization of the syndesmosis but have the advantage that screw removal is unnecessary. A recently published review compared the results of bioabsorbable and metallic syndesmotic screws^[38]. Bioabsorbable syndesmotic screws and metallic syndesmotic screws were comparable with respect to the incidence of complications and range of motion. However, the absolute number of complications was greater with bioabsorbable screws (23.4% vs 5.7%). Most frequent complications of bioabsorbable screws were wound-related complications in 19.7% of the patients.

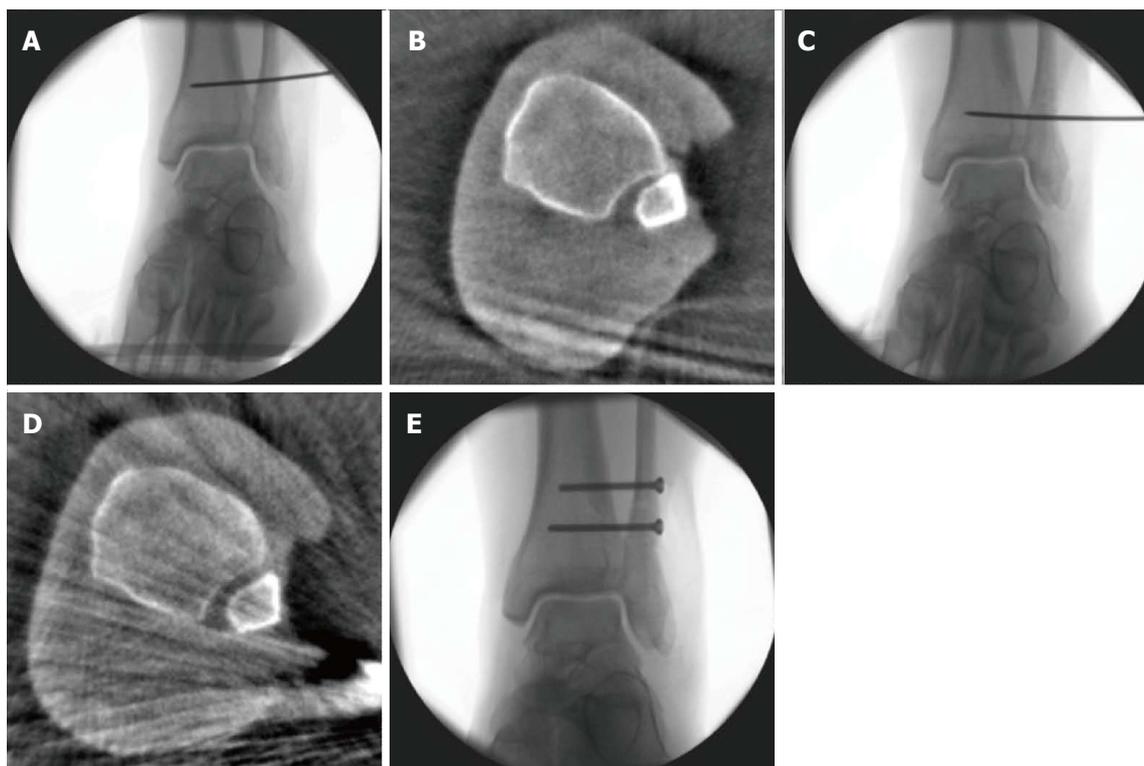


Figure 8 A 25-year-old patient with a Maisonneuve injury. Assessment of reduction with intra-operative three-dimensional scan (A-E): After closed reduction and temporary fixation with a k-wire (A) the three-dimensional scan shows malreduction of the distal fibula in the incisura (B). Immediate intraoperative revision was performed (C) with repeated intraoperative three-dimensional scan showing correct reduction of the distal fibula. With k-wire in place, two syndesmotic screws have been placed to stabilize the ankle diastase (E).

Currently, debate exists over rigid screw fixation vs suture button techniques as the ideal fixation method. The theoretical advantages of a suture-button device over metallic syndesmotic screws are that it allows physiologic motion at the syndesmosis while maintaining the reduction, less risk of hardware pain and subsequent implant removal, and it may permit earlier return to motion as there is no risk of screw breakage and subsequent recurrent syndesmotic diastasis^[41]. In a cadaveric study, Teramoto *et al*^[42] sequentially assessed native syndesmosis ligament stability, suture button, and screw fixation for diastasis in six anatomic specimens. With anatomically directed fixation, there was no significant difference in diastasis for any fixation technique compared with the intact native ligaments. However, screw fixation provided the most rigid fixation and greatest stability against external rotation force.

In the last two decades, many authors have sought to compare suture button techniques vs rigid fixation with cortical screws^[26]. To date, for isolated unstable syndesmosis injuries, no study has shown suture button techniques to be inferior to rigid fixation with regard to joint stability and patient satisfaction.

The use of the Tightrope as fixation method of the ankle diastases has been developed recently. Naqvi *et al*^[43] reported on their experience with 49 patients who were stabilized with the Tightrope device, and found satisfactory clinical results after 2 years of follow-up. One major advantage of this method compared

to screws is that there is no need to remove the knot routinely. A potential limitation of this technique might be the higher costs compared to the screws and, some authors have reported soft tissue irritation from the knot with the need for revision surgery^[44]. According to current literature, the functional outcome is comparable using either Tightrope or syndesmotic screws as fixation device. Detailed analysis of both groups revealed that the Tightrope device was superior to syndesmotic screws regarding the time to return to work. In addition, fewer patients needed implant removal after Tightrope fixation of the syndesmotic diastasis. Recently, a prospective randomized controlled study was published to compare syndesmosis screw and TightRope fixation in terms of accuracy and maintenance of syndesmosis reduction using intraoperative 3D imaging and postoperative bilateral computed tomography (CT)^[45]. No difference was found regarding reduction of the syndesmosis. At two-year follow-up the incidence of ankle joint osteoarthritis and functional outcome showed no difference between the fixation methods.

Intraoperative assessment of reduction of syndesmosis

Several cadaveric studies have demonstrated that standard radiographic measurements used to evaluate the integrity of the syndesmosis are inaccurate and unreliable^[46-48]. Multiple articles have described malreduction after operative treatment in up to 50% of the cases^[46,49]. Even under direct visualization of the

syndesmotic region malreduction has been reported in about 15% because of missing anatomical landmarks^[50-52]. A CT scan allows better visualization of the transverse relationship between the fibula and incisura fibularis^[53-55].

Accuracy of reduction has been shown to correlate with poorer outcome and the development of post-traumatic arthritis^[56-58]. Therefore, some authors advocate the use of a CT scan routinely after operative stabilization of syndesmotic diastasis^[59]. Gardner *et al*^[46] reported on 25 patients who underwent open reduction of a syndesmotic diastasis, and postoperative CT scans showed that 52% of the patients had a malreduced fibula within the incisura.

One possible solution to overcome these problems might be the routine use of intraoperative three-dimensional imaging, as this will allow anatomical fixation of the syndesmosis and immediate intraoperative revision in the case of malreduction. Franke *et al*^[3] investigated a study with the routine use of the intraoperative three-dimensional scan for the assessment of accuracy of syndesmosis reduction in 251 patients. After closed reduction and fixation of the syndesmosis with a 3.5 mm syndesmosis screw, a conventional check of the ankle joint by fluoroscopy in the three standard views was performed. Only if the findings on fluoroscopy showed an adequate reduction by the surgeon's impression an intraoperative three-dimensional scan was performed. In 82 patients (32.7%), malreduction of the syndesmosis was found on the three-dimensional scan despite the fact that the fracture appeared to be adequately reduced on fluoroscopy. After immediate intraoperative revision(s), a repeated intraoperative three-dimensional scan showed anatomical reduction of the syndesmosis.

Examples of intraoperative assessment of syndesmotic reduction with an intraoperative three-dimensional scan are shown in Figure 8.

CONCLUSION

Syndesmotic injuries are common lesions after ankle sprain and require careful examination and management. A displaced and widened mortise requires operative fixation of the syndesmosis. Variable fixation techniques have been reported with comparable results. Furthermore, accuracy of reduction of the syndesmosis is of great concern, as it has been shown to correlate with poorer outcome and the development of post-traumatic osteoarthritis. In view of the high percentage of patients with malreduction of the syndesmosis, intraoperative three-dimensional imaging may be a solution for overcoming this problem. Alternatively, a postoperative CT scan should be performed to assess appropriate reduction.

REFERENCES

- 1 **Egol KA**, Pahl B, Walsh M, Tejwani NC, Davidovitch RI, Koval KJ. Outcome after unstable ankle fracture: effect of syndesmotic stabilization. *J Orthop Trauma* 2010; **24**: 7-11 [PMID: 20035171 DOI: 10.1097/BOT.0b013e3181b1542c]
- 2 **Stark E**, Tornetta P, Creevy WR. Syndesmotic instability in Weber

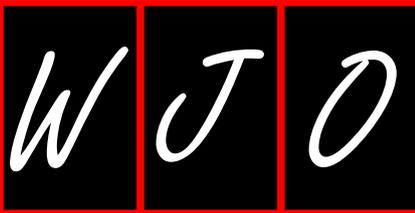
- B ankle fractures: a clinical evaluation. *J Orthop Trauma* 2007; **21**: 643-646 [PMID: 17921840 DOI: 10.1097/BOT.0b013e318157a63a]
- 3 **Franke J**, von Recum J, Suda AJ, Grützner PA, Wendl K. Intraoperative three-dimensional imaging in the treatment of acute unstable syndesmotic injuries. *J Bone Joint Surg Am* 2012; **94**: 1386-1390 [PMID: 22854991 DOI: 10.2106/jbjs.k.01122]
- 4 **Boytim MJ**, Fischer DA, Neumann L. Syndesmotic ankle sprains. *Am J Sports Med* 1991; **19**: 294-298 [PMID: 1907807 DOI: 10.1177/036354659101900315]
- 5 **Hopkinson WJ**, St Pierre P, Ryan JB, Wheeler JH. Syndesmosis sprains of the ankle. *Foot Ankle* 1990; **10**: 325-330 [PMID: 2113510 DOI: 10.1177/107110079001000607]
- 6 **Magan A**, Golano P, Maffulli N, Khanduja V. Evaluation and management of injuries of the tibiofibular syndesmosis. *Br Med Bull* 2014; **111**: 101-115 [PMID: 25190761 DOI: 10.1093/bmb/ldu020]
- 7 **McCullum GA**, van den Bekerom MP, Kerkhoffs GM, Calder JD, van Dijk CN. Syndesmosis and deltoid ligament injuries in the athlete. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1328-1337 [PMID: 23052109 DOI: 10.1007/s00167-012-2205-1]
- 8 **Beumer A**, Valstar ER, Garling EH, Niesing R, Ginai AZ, Ranstam J, Swierstra BA. Effects of ligament sectioning on the kinematics of the distal tibiofibular syndesmosis: a radiostereometric study of 10 cadaveric specimens based on presumed trauma mechanisms with suggestions for treatment. *Acta Orthop* 2006; **77**: 531-540 [PMID: 16819696 DOI: 10.1080/17453670610012557]
- 9 **Xenos JS**, Hopkinson WJ, Mulligan ME, Olson EJ, Popovic NA. The tibiofibular syndesmosis. Evaluation of the ligamentous structures, methods of fixation, and radiographic assessment. *J Bone Joint Surg Am* 1995; **77**: 847-856 [PMID: 7782357]
- 10 **Lauge-hansen N**. Fractures of the ankle. II. Combined experimental-surgical and experimental-roentgenologic investigations. *Arch Surg* 1950; **60**: 957-985 [PMID: 15411319 DOI: 10.1001/archsurg.1950.01250010980011]
- 11 **Wuest TK**. Injuries to the Distal Lower Extremity Syndesmosis. *J Am Acad Orthop Surg* 1997; **5**: 172-181 [PMID: 10797219 DOI: 10.5435/00124635-199705000-00006]
- 12 **Zalavras C**, Thordarson D. Ankle syndesmotic injury. *J Am Acad Orthop Surg* 2007; **15**: 330-339 [PMID: 17548882 DOI: 10.5435/00124635-200706000-00002]
- 13 **van den Bekerom MP**, Lamme B, Hogervorst M, Bolhuis HW. Which ankle fractures require syndesmotic stabilization? *J Foot Ankle Surg* 2007; **46**: 456-463 [PMID: 17980843 DOI: 10.1053/j.jfas.2007.08.009]
- 14 **Alonso A**, Khoury L, Adams R. Clinical tests for ankle syndesmosis injury: reliability and prediction of return to function. *J Orthop Sports Phys Ther* 1998; **27**: 276-284 [PMID: 9549711 DOI: 10.2519/jospt.1998.27.4.276]
- 15 **Beumer A**, Swierstra BA, Mulder PG. Clinical diagnosis of syndesmotic ankle instability: evaluation of stress tests behind the curtains. *Acta Orthop Scand* 2002; **73**: 667-669 [PMID: 12553515 DOI: 10.1080/000164702321039642]
- 16 **Müller ME**, Koch P, Nazarian S, Schatzker J. The comprehensive classification of fractures of long bones. Berlin: Springer-Verlag, 1990 [DOI: 10.1007/978-3-642-61261-9]
- 17 **Harper MC**. Ankle fracture classification systems: a case for integration of the Lauge-Hansen and AO-Danis-Weber schemes. *Foot Ankle* 1992; **13**: 404-407 [PMID: 1427532 DOI: 10.1177/107110079201300708]
- 18 **Park JW**, Kim SK, Hong JS, Park JH. Anterior tibiofibular ligament avulsion fracture in weber type B lateral malleolar fracture. *J Trauma* 2002; **52**: 655-659 [PMID: 11956378 DOI: 10.1097/00005373-200204000-00007]
- 19 **Dias LS**, Giegerich CR. Fractures of the distal tibial epiphysis in adolescence. *J Bone Joint Surg Am* 1983; **65**: 438-444 [PMID: 6833316]
- 20 **Hermans JJ**, Wentink N, Beumer A, Hop WC, Heijboer MP, Moonen AF, Ginai AZ. Correlation between radiological assessment of acute ankle fractures and syndesmotic injury on MRI. *Skeletal Radiol* 2012; **41**: 787-801 [PMID: 22012479 DOI: 10.1007/

- s00256-011-1284-2]
- 21 **Brown KW**, Morrison WB, Schweitzer ME, Parellada JA, Nothnagel H. MRI findings associated with distal tibiofibular syndesmosis injury. *AJR Am J Roentgenol* 2004; **182**: 131-136 [PMID: 14684526 DOI: 10.2214/ajr.182.1.1820131]
 - 22 **Hermans JJ**, Beumer A, Hop WC, Moonen AF, Ginai AZ. Tibiofibular syndesmosis in acute ankle fractures: additional value of an oblique MR image plane. *Skeletal Radiol* 2012; **41**: 193-202 [PMID: 21533651 DOI: 10.1007/s00256-011-1179-2]
 - 23 **van den Bekerom MP**, Mutsaerts EL, van Dijk CN. Evaluation of the integrity of the deltoid ligament in supination external rotation ankle fractures: a systematic review of the literature. *Arch Orthop Trauma Surg* 2009; **129**: 227-235 [PMID: 18953550 DOI: 10.1007/s00402-008-0768-6]
 - 24 **Lui TH**, Ip K, Chow HT. Comparison of radiologic and arthroscopic diagnoses of distal tibiofibular syndesmosis disruption in acute ankle fracture. *Arthroscopy* 2005; **21**: 1370 [PMID: 16325090 DOI: 10.1016/j.arthro.2005.08.016]
 - 25 **van Dijk CN**, Longo UG, Loppini M, Florio P, Maltese L, Ciuffreda M, Denaro V. Conservative and surgical management of acute isolated syndesmotic injuries: ESSKA-AFAS consensus and guidelines. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 1217-1227 [PMID: 26846658 DOI: 10.1007/s00167-016-4017-1]
 - 26 **Miller TL**, Skalak T. Evaluation and treatment recommendations for acute injuries to the ankle syndesmosis without associated fracture. *Sports Med* 2014; **44**: 179-188 [PMID: 24127279 DOI: 10.1007/s40279-013-0106-1]
 - 27 **Amendola A**, Williams G, Foster D. Evidence-based approach to treatment of acute traumatic syndesmosis (high ankle) sprains. *Sports Med Arthrosc* 2006; **14**: 232-236 [PMID: 17135973 DOI: 10.1097/01.jsa.0000212329.32969.b8]
 - 28 **Fritschy D**. An unusual ankle injury in top skiers. *Am J Sports Med* 1989; **17**: 282-285 [PMID: 2502928 DOI: 10.1177/036354658901700223]
 - 29 **Nussbaum ED**, Hosea TM, Sieler SD, Incremona BR, Kessler DE. Prospective evaluation of syndesmotic ankle sprains without diastasis. *Am J Sports Med* 2001; **29**: 31-35 [PMID: 11206253]
 - 30 **Taylor DC**, Englehardt DL, Bassett FH. Syndesmosis sprains of the ankle. The influence of heterotopic ossification. *Am J Sports Med* 1992; **20**: 146-150 [PMID: 1558241 DOI: 10.1177/036354659202000209]
 - 31 **Taylor DC**, Tenuta JJ, Uhorchak JM, Arciero RA. Aggressive surgical treatment and early return to sports in athletes with grade III syndesmosis sprains. *Am J Sports Med* 2007; **35**: 1833-1838 [PMID: 17644659 DOI: 10.1177/0363546507304666]
 - 32 **Hunt KJ**, Phisitkul P, Pirollo J, Amendola A. High Ankle Sprains and Syndesmotic Injuries in Athletes. *J Am Acad Orthop Surg* 2015; **23**: 661-673 [PMID: 26498585 DOI: 10.5435/jaaos-d-13-00135]
 - 33 **Schepers T**, van Zuuren WJ, van den Bekerom MP, Vogels LM, van Lieshout EM. The management of acute distal tibiofibular syndesmotic injuries: results of a nationwide survey. *Injury* 2012; **43**: 1718-1723 [PMID: 22795845 DOI: 10.1016/j.injury.2012.06.015]
 - 34 **Thompson MC**, Gesink DS. Biomechanical comparison of syndesmosis fixation with 3.5- and 4.5-millimeter stainless steel screws. *Foot Ankle Int* 2000; **21**: 736-741 [PMID: 11023220]
 - 35 **Beumer A**, Campo MM, Niesing R, Day J, Kleinrensink GJ, Swierstra BA. Screw fixation of the syndesmosis: a cadaver model comparing stainless steel and titanium screws and three and four cortical fixation. *Injury* 2005; **36**: 60-64 [PMID: 15589915 DOI: 10.1016/j.injury.2004.05.024]
 - 36 **McBryde A**, Chiasson B, Wilhelm A, Donovan F, Ray T, Bacilla P. Syndesmotic screw placement: a biomechanical analysis. *Foot Ankle Int* 1997; **18**: 262-266 [PMID: 9167924 DOI: 10.1177/107110079701800503]
 - 37 **Kaftandziev I**, Spasov M, Trpeski S, Zafirova-Ivanovska B, Bakota B. Fate of the syndesmotic screw--Search for a prudent solution. *Injury* 2015; **46** Suppl 6: S125-S129 [PMID: 26582218 DOI: 10.1016/j.injury.2015.10.062]
 - 38 **van der Eng DM**, Schep NW, Schepers T. Bioabsorbable Versus Metallic Screw Fixation for Tibiofibular Syndesmotic Ruptures: A Meta-Analysis. *J Foot Ankle Surg* 2015; **54**: 657-662 [PMID: 25960058 DOI: 10.1053/j.jfas.2015.03.014]
 - 39 **Andersen MR**, Frihagen F, Madsen JE, Figved W. High complication rate after syndesmotic screw removal. *Injury* 2015; **46**: 2283-2287 [PMID: 26319204 DOI: 10.1016/j.injury.2015.08.021]
 - 40 **Schepers T**. To retain or remove the syndesmotic screw: a review of literature. *Arch Orthop Trauma Surg* 2011; **131**: 879-883 [PMID: 21161662 DOI: 10.1007/s00402-010-1225-x]
 - 41 **Schepers T**. Acute distal tibiofibular syndesmosis injury: a systematic review of suture-button versus syndesmotic screw repair. *Int Orthop* 2012; **36**: 1199-1206 [PMID: 22318415 DOI: 10.1007/s00264-012-1500-2]
 - 42 **Teramoto A**, Suzuki D, Kamiya T, Chikenji T, Watanabe K, Yamashita T. Comparison of different fixation methods of the suture-button implant for tibiofibular syndesmosis injuries. *Am J Sports Med* 2011; **39**: 2226-2232 [PMID: 21768530 DOI: 10.1177/0363546511413455]
 - 43 **Naqvi GA**, Shafqat A, Awan N. Tightrope fixation of ankle syndesmosis injuries: clinical outcome, complications and technique modification. *Injury* 2012; **43**: 838-842 [PMID: 22036451 DOI: 10.1016/j.injury.2011.10.002]
 - 44 **Qamar F**, Kadakia A, Venkateswaran B. An anatomical way of treating ankle syndesmotic injuries. *J Foot Ankle Surg* 2011; **50**: 762-765 [PMID: 21962383 DOI: 10.1053/j.jfas.2011.07.001]
 - 45 **Kortekangas T**, Savola O, Flinkkilä T, Lepojärvi S, Nortunen S, Ohtonen P, Katisko J, Pakarinen H. A prospective randomised study comparing TightRope and syndesmotic screw fixation for accuracy and maintenance of syndesmotic reduction assessed with bilateral computed tomography. *Injury* 2015; **46**: 1119-1126 [PMID: 25769201 DOI: 10.1016/j.injury.2015.02.004]
 - 46 **Gardner MJ**, Demetrakopoulos D, Briggs SM, Helfet DL, Lorich DG. Malreduction of the tibiofibular syndesmosis in ankle fractures. *Foot Ankle Int* 2006; **27**: 788-792 [PMID: 17054878]
 - 47 **Nielson JH**, Gardner MJ, Peterson MG, Sallis JG, Potter HG, Helfet DL, Lorich DG. Radiographic measurements do not predict syndesmotic injury in ankle fractures: an MRI study. *Clin Orthop Relat Res* 2005; **(436)**: 216-221 [PMID: 15995444]
 - 48 **Beumer A**, van Hemert WL, Niesing R, Entius CA, Ginai AZ, Mulder PG, Swierstra BA. Radiographic measurement of the distal tibiofibular syndesmosis has limited use. *Clin Orthop Relat Res* 2004; **(423)**: 227-234 [PMID: 15232454]
 - 49 **Marmor M**, Hansen E, Han HK, Buckley J, Matityahu A. Limitations of standard fluoroscopy in detecting rotational malreduction of the syndesmosis in an ankle fracture model. *Foot Ankle Int* 2011; **32**: 616-622 [PMID: 21733425 DOI: 10.3113/fai.2011.0616]
 - 50 **Miller AN**, Carroll EA, Parker RJ, Boraiah S, Helfet DL, Lorich DG. Direct visualization for syndesmotic stabilization of ankle fractures. *Foot Ankle Int* 2009; **30**: 419-426 [PMID: 19439142 DOI: 10.3113/fai.2009.0419]
 - 51 **Sagi HC**, Shah AR, Sanders RW. The functional consequence of syndesmotic joint malreduction at a minimum 2-year follow-up. *J Orthop Trauma* 2012; **26**: 439-443 [PMID: 22357084 DOI: 10.1097/BOT.0b013e31822a526a]
 - 52 **Lilyquist M**, Shaw A, Latz K, Bogener J, Wentz B. Cadaveric Analysis of the Distal Tibiofibular Syndesmosis. *Foot Ankle Int* 2016; **37**: 882-890 [PMID: 27060126 DOI: 10.1177/1071100716643083]
 - 53 **Laflamme M**, Belzile EL, Bédard L, van den Bekerom MP, Glazebrook M, Pelet S. A prospective randomized multicenter trial comparing clinical outcomes of patients treated surgically with a static or dynamic implant for acute ankle syndesmosis rupture. *J Orthop Trauma* 2015; **29**: 216-223 [PMID: 25260059 DOI: 10.1097/bot.0000000000000245]
 - 54 **Malhotra G**, Cameron J, Toolan BC. Diagnosing chronic diastasis of the syndesmosis: a novel measurement using computed tomography. *Foot Ankle Int* 2014; **35**: 483-488 [PMID: 24505045 DOI: 10.1177/1071100714523273]
 - 55 **Mukhopadhyay S**, Metcalfe A, Guha AR, Mohanty K, Hemmadi

- S, Lyons K, O'Doherty D. Malreduction of syndesmosis--are we considering the anatomical variation? *Injury* 2011; **42**: 1073-1076 [PMID: 21550047 DOI: 10.1016/j.injury.2011.03.019]
- 56 **Yablon IG**, Leach RE. Reconstruction of malunited fractures of the lateral malleolus. *J Bone Joint Surg Am* 1989; **71**: 521-527 [PMID: 2703512]
- 57 **Chissell HR**, Jones J. The influence of a diastasis screw on the outcome of Weber type-C ankle fractures. *J Bone Joint Surg Br* 1995; **77**: 435-438 [PMID: 7744931]
- 58 **Weening B**, Bhandari M. Predictors of functional outcome following transsyndesmotic screw fixation of ankle fractures. *J Orthop Trauma* 2005; **19**: 102-108 [PMID: 15677926 DOI: 10.1097/00005131-200502000-00006]
- 59 **Taser F**, Shafiq Q, Ebraheim NA. Three-dimensional volume rendering of tibiofibular joint space and quantitative analysis of change in volume due to tibiofibular syndesmosis diastases. *Skeletal Radiol* 2006; **35**: 935-941 [PMID: 16683157 DOI: 10.1007/s00256-006-0101-9]

P- Reviewer: Anand A, Fanter NJ, Ohishi T, Zhen P **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Lu YJ





Vitamin D and spine surgery

Thomas Mabey, Weerasak Singhatanadgige, Wicharn Yingsakmongkol, Worawat Limthongkul, Sittisak Honsawek

Thomas Mabey, Sittisak Honsawek, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Weerasak Singhatanadgige, Wicharn Yingsakmongkol, Worawat Limthongkul, Sittisak Honsawek, Vinai Parkpian Orthopaedic Research Center, Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Thomas Mabey, Weerasak Singhatanadgige, Wicharn Yingsakmongkol, Worawat Limthongkul, Sittisak Honsawek, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok 10330, Thailand

Author contributions: Mabey T collected, analyzed, and drafted the manuscript; Singhatanadgige W, Yingsakmongkol W, Limthongkul W provided the technical support; Honsawek S provided administrative support, the input in writing the paper and coordinated the writing of the paper.

Conflict-of-interest statement: There is no conflict of interest associated with coauthors contributed their efforts in this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Sittisak Honsawek, MD, PhD, Vinai Parkpian Orthopaedic Research Center, Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, Rama IV road, Patumwan, Bangkok 10330, Thailand. sittisak.h@chula.ac.th
Telephone: +66-2-2564482
Fax: +66-2-2564482

Received: May 5, 2016

Peer-review started: May 9, 2016

First decision: July 14, 2016

Revised: August 9, 2016

Accepted: August 30, 2016

Article in press: August 31, 2016

Published online: November 18, 2016

Abstract

Vitamin D is crucial for musculoskeletal health, maintenance, and function. Vitamin D insufficiency is common among patients undergoing spine surgery and the ideal vitamin D level for spine surgery has yet to be investigated. There is a high prevalence of hypovitaminosis D in patients with musculoskeletal pain regardless of surgical intervention. With the frequency and costs of spine surgery increasing, it is imperative that efforts are continued to reduce the impact on patients and healthcare services. Studies into vitamin D and its associations with orthopaedic surgery have yielded alarming findings with regards to the prevalence of vitamin D deficiency. Importantly, altered vitamin D status also contributes to a wide range of disease conditions. Therefore, future investigations are still essential for better understanding the relationship between vitamin D and spine surgery outcomes. Whilst further research is required to fully elucidate the extent of the effects of hypovitaminosis D has on surgical outcomes, it is strongly advisable to reduce the impacts by appropriate vitamin D supplementation of deficient and at-risk patients.

Key words: Hypovitaminosis D; Outcome; Prevalence; Spine surgery; Vitamin D

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A growing body of evidence suggests that vitamin D plays an essential role in skeletal development,

bone remodeling, fracture repair, and muscle strength. Vitamin D deficiency is highly prevalent in the elderly and underestimated by spine surgeons. Studies into vitamin D and its associations with orthopaedic surgery have yielded alarming findings with regards to the prevalence of vitamin D deficiency. Importantly, altered vitamin D status also contributes to a wide range of disease conditions and surgical outcome. Therefore, further investigations are still essential for better understanding paradoxical relationship between vitamin D status and spine surgery outcome.

Mabey T, Singhatanadgige W, Yingsakmongkol W, Limthongkul W, Honsawek S. Vitamin D and spine surgery. *World J Orthop* 2016; 7(11): 726-730 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/726.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.726>

INTRODUCTION

A growing body of evidence suggests that vitamin D plays an essential role in skeletal development, bone remodeling, fracture repair, and muscle strength. Vitamin D deficiency is highly prevalent in the elderly and underestimated by spine surgeons. With the frequency and costs of spine surgery increasing, it is imperative that efforts are continued to reduce the impact on patients and healthcare services. Studies into vitamin D and its associations with orthopaedic surgery have yielded alarming results with regards to the prevalence of vitamin D deficiency. Generally speaking, serum 25-hydroxyvitamin D [25(OH)D] concentrations of less than 20 ng/mL are considered insufficient and below 10 ng/mL are deficient. However, there is still no standardised definition of where hypovitaminosis D starts, in part because of the conflicting data. What is largely agreed on though is that alarming numbers of the global population have insufficient vitamin D levels.

Vitamin D acts *via* the vitamin D receptor (VDR) on a range of tissues where it has multiple effects (reviewed in detail by Hossein-nezhad *et al.*^[1]). Perhaps most well-known is the way in which activated vitamin D acts on the kidneys and intestines to regulate calcium and phosphorus concentrations in the blood. In addition to this vital function, vitamin D is well known for its involvement in bone metabolism^[2]. The induction of both bone formation and remodelling seems at first glance to be somewhat paradoxical. However, there exists strong links between bone mineral density (BMD) and vitamin D levels.

As we explore below, surgical outcomes are hindered by low vitamin D levels. Complications including recurrent fractures, insufficient tissue repair, and loosening of surgical hardware often require further surgeries and therapeutic intervention to ameliorate. Using simple and reasonable measures through the administration of vitamin D supplementation to reduce

these effects would be a logical step in the continued effort to improve patient care and minimise financial expenditures.

VITAMIN D IN SPINE SURGERY

Despite the frequency of spinal surgery, particularly in elderly patients, there is a scarcity of research on vitamin D levels and surgical outcomes. However, a number of case studies have indicated the importance of healthy vitamin D levels. In two cases of severe hypovitaminosis D unsuccessful outcomes of spinal fusion surgery were observed, but following high vitamin D supplementation patients improved^[3]. Likewise, a 76-year-old female with osteoporosis and circulating 25(OH)D levels of 9 ng/mL suffered compression fractures in thoracic and lumbar vertebrae. Following kyphoplasty, the patient reported no improvement in pain and suffered a further lumbar compression fracture, whereafter she received 2200 IU/d of vitamin D supplementation. Impressive clinical improvements were noted in muscle strength and a decrease in back pain^[4]. This is supported by a study of 40 patients with acute symptomatic vertebral compression fractures who underwent kyphoplasty surgery^[5]. When investigating the recurrence rate of fractures, serum 25(OH)D concentrations were higher in patients with no new fractures post-operatively compared with those who had suffered additional fractures, but lumbar BMD scores showed no significant difference. Schwalfenberg^[6] reported 6 cases of improvements in back pain and failed back surgery patients through vitamin D supplementation. Patients respond over a range of time frames from 3 to 6 wk and whilst all patients showed improvements in pain, some responded better to treatment. It is suggested that 4000-5000 IU/d of vitamin D supplements may be required to improve the patients' conditions. An interesting observation was the improvement in mood noted in some cases, whether through direct psychoactive effects of vitamin D or as a result of decreased pain; it is another aspect to consider when evaluating vitamin D.

Moreover, Waikakul^[7] investigated the association of serum 25(OH)D levels with pain and low back function in patients with failed back surgery syndrome. Of the nine cases, an initial 20000 IU loading dose of ergocalciferol, followed by daily doses of 600 IU of cholecalciferol showed improvements in all but one patient for pain and Japanese Orthopaedic Association (JOA) back scores. At 6 mo follow-up, patients continued to improve with just 2 experiencing only slight improvements. It suggests that high loading doses followed by prolonged use of maintenance doses can improve the functional scores of patients. Supporting this, a longitudinal study of 360 idiopathic low back pain patients in Saudi Arabia found that, at baseline, only 17% had normal vitamin D levels^[8]. Patients were given high doses of vitamin D (5000-10000 IU/d) for 3 mo. At follow up 95% of patients reported the disappearance of low back pain and all patients had gained normal serum 25(OH)D

levels. Finally, in a prospective follow-up study of 31 females undergoing posterior decompression surgery and instrumented posterolateral fusion for lumbar spinal stenosis, post-operative (1 year follow-up) vitamin D levels were positively correlated with surgery outcome scores. The authors also remark the high prevalence of deficient vitamin D levels in lumbar spinal stenosis patients^[9]. These reports showcase the risks to surgical outcomes of hypovitaminosis D, but also the possible benefits of vitamin D supplementation. High and maintained vitamin D treatment appears to be effective at both ameliorating surgical procedures, for example bone grafts and hardware fusion, and patients' symptoms including pain, function, and mood, which in turn often alleviates the need for analgesics.

A number of studies have reported alarmingly high prevalences of insufficient or deficient vitamin D levels in orthopaedic spine patients. A retrospective study of 313 adults undergoing spinal fusion by Stoker *et al.*^[10] found circulating 25(OH)D concentrations in nearly 90% of patients were insufficient or deficient (< 30 ng/mL); 3.5% were classified as severely deficient (< 10 ng/mL). Whilst females are often regarded as being at higher risk of hypovitaminosis D; no difference was observed between male and female patients, though vitamin D deficient patients tended to have higher pain and worse disability scores. Similarly, when Kim *et al.*^[11] examined vitamin D levels in 350 lumbar spinal stenosis patients with chronic low back pain and leg pain, they found that there was a high prevalence of hypovitaminosis D, only 2.9% of participants being vitamin D sufficient (> 30 ng/mL). Vitamin D deficiency was associated with both low back pain and leg pain in addition to sun light exposure. Furthermore, in Norway, a study of 572 patients complaining of headaches, fatigue, and musculoskeletal pain observed a high prevalence of vitamin D deficiency. The prevalence was affected by ethnicity; 83% of South Asian and African patients, but only 35% of native Norwegian patients were hypovitaminosis D sufferers^[12].

In a cross sectional study of 400 individuals, there was a positive association between vitamin D levels and low BMD in both males and females that was independent of age, although vitamin D deficient participants were older than those with normal levels. Of the deficient participants, 100% had lumbar and hip BMD scores in the range of osteopenia or consistent with osteoporosis^[13]. Whilst age is a recognised risk factor of vitamin D deficiency, younger patients should not be assumed to have healthy levels as shown by a study of the 70 paediatric orthopaedic patients undergoing long bone osteotomies, hip osteotomies, and spinal fusions studied by Parry *et al.*^[14], 90% of whom had subnormal vitamin D concentrations with 16% being severely deficient (< 12 ng/mL). Cholecystectomy put spine patients at an increased risk of vitamin D deficiency^[15]. When classified into two groups - those who had previously undergone a cholecystectomy and those who had not - 40.8% of previous cholecystectomy patients

were vitamin D deficient (< 20 ng/mL) compared to 25% of non-cholecystectomy patients. The aforementioned studies suggest the need to identify at-risk patients, particularly older patients and those who have histories of low bone density or medical conditions affecting bone metabolism.

Lumbar spine BMD has been shown to be decreased in low vitamin D patients as shown by the lumbar BMD scores of physically active and normal adolescent females in Israel which showed all participants were vitamin D insufficient (< 30 ng/mL) with 64% being defined as deficient (< 14 ng/mL). Furthermore, activity is associated with lumbar BMD and BMD scores are most strongly associated with the lowest tertile of 25(OH)D levels^[16]. However, in Swiss teenagers with appendicular fractures, there was no difference between healthy individuals and those with fractures in vitamin D levels or lumbar or heel BMD, nor was there a difference between fracture sites. Despite a high prevalence of hypovitaminosis D, there was no association between vitamin D levels and spinal BMD^[17]. Low BMD increases the risk of failure in surgical procedures, especially the application of hardware, for instance in spinal fusion. The vitamin D levels of patients, principally the elderly, should be maintained at satisfactory levels prior to and proceeding surgeries. Equally important is the activity of patients. Excessive and unnecessary use of back support braces can lead to weakening of the supportive muscles in the back, which in turn can lead to pain and less successful surgical outcomes. It should also be noted that genetic factors may contribute to the outcome of spine surgery. VDR gene polymorphisms were investigated by in a cross-sectional study of 318 postmenopausal females in Japan indicated that a VDR haplotype was associated with the severity of spondylosis in lumbar spine^[18].

A retrospective investigation of orthopaedic patients undergoing cervical, thoracic, and lumbar disk replacements, decompressions, and arthroplasty revealed vitamin D deficiency (< 20 ng/mL) to be associated with cervical disk herniation, in particular, the number of herniations. The likelihood of disc herniation was higher in patients with lower vitamin D levels^[19]. Research has been focused on investigating possible relationships between vitamin D status and clinical outcome in patients with spine surgery, as summarized in Table 1.

There is a disturbingly high prevalence of hypovitaminosis D in orthopaedic patients around the world. Low vitamin D levels appear to be the cause of many failed spinal surgeries, but despite the importance, and apparent severity, little research has been performed on the associations with surgical outcomes. With the relative inexpensiveness and safety of vitamin D supplementation, it would be prudent to screen for low circulating 25(OH)D concentrations and treat those found to be insufficient in an attempt to increase the chances of successful procedural outcomes.

Low vitamin D status is associated with a variety

Table 1 Summary of studies of vitamin status in patients with spine surgery

Ref.	Study design	Subjects	Significance
Schwalfenberg ^[6] , 2009	Case series	6 patients with chronic back pain and failed back surgery	Repletion of inadequate vitamin D levels shows significant improvement or complete resolution of chronic low back pain symptoms
Pneumaticos <i>et al</i> ^[4] , 2011	Case series	1 patient with osteoporosis with lumbar compression fracture	After kyphoplasty, vitamin D supplementation can improve muscle strength and decrease back pain
Waikakul ^[7] , 2012	Retrospective study	9 patients with failed back surgery syndrome	Vitamin D supplementation can improve the functional scores of patients with failed back surgery syndrome
Zafeiris <i>et al</i> ^[5] , 2012	Prospective longitudinal study	40 postmenopausal women with vertebral compression fractures	Patients with recurrent fractures have lower vitamin D levels than patients without recurrent fractures after kyphoplasty
Kim <i>et al</i> ^[9] , 2012	Prospective study	31 female patients with lumbar spinal stenosis	Vitamin D deficiency is common in lumbar spinal stenosis patients and postoperative vitamin D is significantly correlated with surgical outcomes
Kim <i>et al</i> ^[11] , 2013	Cross-sectional study	350 patients with lumbar spinal stenosis	Vitamin D deficiency is highly prevalent in lumbar spinal stenosis patients and is associated with severe pain
Stoker <i>et al</i> ^[10] , 2013	Cross-sectional study	313 patients with degenerative spondylosis	There is a substantially high prevalence of hypovitaminosis D in patients undergoing spinal fusion
Stoker <i>et al</i> ^[9] , 2013	Retrospective study	91 patients: 74 herniation, 17 no herniation	Vitamin D deficiency is associated with cervical disk herniation

of adverse outcomes following surgical procedures. In recent years, previous investigation has documented that serum 25(OH)D level at the time of operation is highly predictive of long term surgical outcomes compared to postoperative vitamin D status, and that benefits can be attained by vitamin D supplementation at the time of surgical procedures or thereafter^[20].

Vitamin D status is a prognosticator of extraskelatal abnormalities for which predispositions could be detected and deficiencies should be corrected before surgical treatments. Our recommendation for patients with vitamin D deficiency prior to elective spine surgery is as follows. In patients whose 25(OH)D is less than 20 ng/mL, treatment generally includes initial 50000 IU loading dose of vitamin D orally once weekly for two to three months, and then 1000 or more IU of vitamin D daily thereafter. After three months, serum 25(OH)D should be reassessed. In patients whose 25(OH)D is 20-30 ng/mL, treatment includes 1000 IU of vitamin D by mouth daily, commonly for a three-month period. However, some patients may require higher doses. The ideal dose of vitamin D is determined by measuring serum 25(OH)D, and increasing the dose if serum vitamin D level is not within the normal range. Once a normal level is achieved, continued therapy with 800 IU of vitamin D daily is generally suggested. Although various strategies could be used in treating vitamin D deficiency, a common overlooking in management is to discontinue treatment or administer inadequate vitamin D maintenance dosing when the serum 25(OH)D level reaches the optimal range. It is, therefore, reasonable to routinely screen all patients undergoing spine fusion surgery for serum 25(OH)D levels, and those with vitamin D deficiency should be given vitamin D supplements.

CONCLUSION

Heretofore, limited research has been conducted into the associations of vitamin D and spine surgical outcomes. However, the existing evidence shows a need to improve

vitamin D levels in patients with unsatisfactory results. There is an alarmingly high prevalence of subnormal vitamin D levels among orthopaedic patients reported in the literature. Considering the detrimental impact of hypovitaminosis D in patients undergoing spine surgery, preoperative vitamin D screening may be needed for those at high risk of deficiency. Whilst further research is required to fully elucidate the extent of the effects of hypovitaminosis D on clinical outcomes, it is strongly advisable to reduce the impacts by appropriate supplementation of deficient and at-risk patients to adequate levels.

ACKNOWLEDGEMENTS

The authors thank the National Research University Project, Office of the Higher Education Commission through the Ageing Cluster (NRU59-056-AS), Chulalongkorn University.

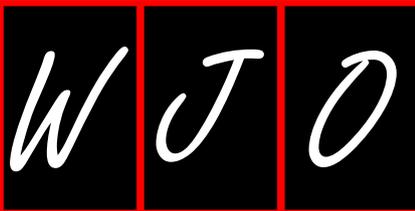
REFERENCES

- 1 **Hosseini-nezhad A**, Holick MF. Vitamin D for health: a global perspective. *Mayo Clin Proc* 2013; **88**: 720-755 [PMID: 23790560 DOI: 10.1016/j.mayocp.2013.05.011]
- 2 **Anderson PH**, Turner AG, Morris HA. Vitamin D actions to regulate calcium and skeletal homeostasis. *Clin Biochem* 2012; **45**: 880-886 [PMID: 22414785 DOI: 10.1016/j.clinbiochem.2012.02.020]
- 3 **Plehwe WE**, Carey RP. Spinal surgery and severe vitamin D deficiency. *Med J Aust* 2002; **176**: 438-439 [PMID: 12056998]
- 4 **Pneumaticos SG**, Zafeiris CP, Chronopoulos E, Kassi E, Lyritis GP. Vitamin D deficiency resulting to a subsequent vertebral fracture after kyphoplasty. *J Musculoskelet Neuronal Interact* 2011; **11**: 81-83 [PMID: 21364277]
- 5 **Zafeiris CP**, Lyritis GP, Papaioannou NA, Gratsias PE, Galanos A, Chatziioannou SN, Pneumaticos SG. Hypovitaminosis D as a risk factor of subsequent vertebral fractures after kyphoplasty. *Spine J* 2012; **12**: 304-312 [PMID: 22494816 DOI: 10.1016/j.spinee.2012.02.016]
- 6 **Schwalfenberg G**. Improvement of chronic back pain or failed back surgery with vitamin D repletion: a case series. *J Am Board Fam Med* 2009; **22**: 69-74 [PMID: 19124636 DOI: 10.3122/

- jabfm.2009.01.080026]
- 7 **Waikakul S.** Serum 25-hydroxy-calciferol level and failed back surgery syndrome. *J Orthop Surg (Hong Kong)* 2012; **20**: 18-22 [PMID: 22535805]
 - 8 **Al Faraj S, Al Mutairi K.** Vitamin D deficiency and chronic low back pain in Saudi Arabia. *Spine (Phila Pa 1976)* 2003; **28**: 177-179 [PMID: 12544936 DOI: 10.1097/00007632-200301150-00015]
 - 9 **Kim TH, Yoon JY, Lee BH, Jung HS, Park MS, Park JO, Moon ES, Kim HS, Lee HM, Moon SH.** Changes in vitamin D status after surgery in female patients with lumbar spinal stenosis and its clinical significance. *Spine (Phila Pa 1976)* 2012; **37**: E1326-E1330 [PMID: 22805343 DOI: 10.1097/BRS.0b013e318268ff05]
 - 10 **Stoker GE, Buchowski JM, Bridwell KH, Lenke LG, Riew KD, Zebala LP.** Preoperative vitamin D status of adults undergoing surgical spinal fusion. *Spine (Phila Pa 1976)* 2013; **38**: 507-515 [PMID: 22986835 DOI: 10.1097/BRS.0b013e3182739ad1]
 - 11 **Kim TH, Lee BH, Lee HM, Lee SH, Park JO, Kim HS, Kim SW, Moon SH.** Prevalence of vitamin D deficiency in patients with lumbar spinal stenosis and its relationship with pain. *Pain Physician* 2013; **16**: 165-176 [PMID: 23511683]
 - 12 **Knutsen KV, Brekke M, Gjelstad S, Lagerlöv P.** Vitamin D status in patients with musculoskeletal pain, fatigue and headache: a cross-sectional descriptive study in a multi-ethnic general practice in Norway. *Scand J Prim Health Care* 2010; **28**: 166-171 [PMID: 20642395 DOI: 10.3109/02813432.2010.505407]
 - 13 **Sadat-Ali M, Al Elq AH, Al-Turki HA, Al-Mulhim FA, Al-Ali AK.** Influence of vitamin D levels on bone mineral density and osteoporosis. *Ann Saudi Med* 2011; **31**: 602-608 [PMID: 22048506 DOI: 10.4103/0256-4947.87097]
 - 14 **Parry J, Sullivan E, Scott AC.** Vitamin D sufficiency screening in preoperative pediatric orthopaedic patients. *J Pediatr Orthop* 2011; **31**: 331-333 [PMID: 21415696 DOI: 10.1097/BPO.0b013e3182104a94]
 - 15 **Stoker GE, Buchowski JM, Stoker ME.** Prior cholecystectomy as a predictor of preoperative vitamin D deficiency in adults undergoing spine surgery. *Arch Surg* 2012; **147**: 577-578 [PMID: 22786550 DOI: 10.1001/archsurg.2012.463]
 - 16 **Constantini NW, Dubnov-Raz G, Chodick G, Rozen GS, Giladi A, Ish-Shalom S.** Physical activity and bone mineral density in adolescents with vitamin D deficiency. *Med Sci Sports Exerc* 2010; **42**: 646-650 [PMID: 19952847 DOI: 10.1249/MSS.0b013e318181bb813b]
 - 17 **Ceroni D, Anderson de la Llana R, Martin X, Lamah L, De Coulon G, Turcot K, Dubois-Ferrière V.** Prevalence of vitamin D insufficiency in Swiss teenagers with appendicular fractures: a prospective study of 100 cases. *J Child Orthop* 2012; **6**: 497-503 [PMID: 24294313 DOI: 10.1007/s11832-012-0446-7]
 - 18 **Koshizuka Y, Ogata N, Shiraki M, Hosoi T, Seichi A, Takeshita K, Nakamura K, Kawaguchi H.** Distinct association of gene polymorphisms of estrogen receptor and vitamin D receptor with lumbar spondylosis in post-menopausal women. *Eur Spine J* 2006; **15**: 1521-1528 [PMID: 16362385 DOI: 10.1007/s00586-005-0005-8]
 - 19 **Stoker GE, Buchowski JM, Chen CT, Kim HJ, Park MS, Riew KD.** Hypovitaminosis D and Cervical Disk Herniation among Adults Undergoing Spine Surgery. *Global Spine J* 2013; **3**: 231-236 [PMID: 24436874 DOI: 10.1055/s-0033-1354252]
 - 20 **Bashutski JD, Eber RM, Kinney JS, Benavides E, Maitra S, Braun TM, Giannobile WV, McCauley LK.** The impact of vitamin D status on periodontal surgery outcomes. *J Dent Res* 2011; **90**: 1007-1012 [PMID: 21555774 DOI: 10.1177/0022034511407771]

P- Reviewer: Alimehmeti R, Elgafy H, Mori K, Teli MGA
S- Editor: Kong JX **L- Editor:** A **E- Editor:** Lu YJ





Basic Study

Three-dimensional reconstructed magnetic resonance scans: Accuracy in identifying and defining knee meniscal tears

Neil Kruger, Eugene McNally, Sami Al-Ali, Raj Rout, Jonathan L Rees, Andrew J Price

Neil Kruger, Orthopaedic Research Unit, University of Cape Town, Cape Town 7925, South Africa

Eugene McNally, Raj Rout, Jonathan L Rees, Andrew J Price, Nuffield Orthopaedic Centre, University of Oxford, Oxford OX3 7LD, United Kingdom

Sami Al-Ali, the Whittington Hospital, London N19 5NF, United Kingdom

Author contributions: Price AJ and Rees JL contributed to study design and concept, proof reading and editing; McNally E contributed to study design, data input and analysis; Al-Ali S and Rout R contributed to data input, analysis, editing and proofing; Kruger N contributed to data input and analysis, study design and wrote the paper.

Institutional review board statement: All scan data was solely maintained on hospital computers and anonymised prior to segmentation, hence independent IRB board approval was not required.

Conflict-of-interest statement: None of the authors have any conflict of interest or anything to disclose related to the research performed.

Data sharing statement: The technical appendix and dataset is available from the corresponding author at neilkruger6@gmail.com. As per the IRB statement, all patient data was kept on hospital computers and anonymised prior to segmentation. Risk of identification is hence extremely low.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Neil Kruger, Orthopaedic Research Unit, Department of Orthopaedics, University of Cape Town, Groote Schuur Hospital, Cape Town 8001, South Africa. neilkruger6@gmail.com
Telephone: +27-21-4045118

Received: January 11, 2016

Peer-review started: January 14, 2016

First decision: March 7, 2016

Revised: July 6, 2016

Accepted: August 17, 2016

Article in press: August 18, 2016

Published online: November 18, 2016

Abstract

AIM

To determine whether three-dimensional (3D) reconstruction from conventional magnetic resonance imaging (MRI) is able to accurately detect a meniscal tear, and define the configuration.

METHODS

Thirty-three patients' 3T MRI scan data were collected and sagittal uni-planar 3D reconstructions performed from the preoperative MRI. There were 24 meniscal tears in 24 patients, and nine controls. All patients had arthroscopic corroboration of MRI findings. Two independent observers prospectively reported on all 33 reconstructions. Meniscal tear presence or absence was noted, and tear configuration subsequently categorised as either radial, bucket-handle, parrot beak, horizontal or complex.

RESULTS

Identification of control menisci or meniscal tear presence was excellent (Accuracy: observer 1 = 90.9%; observer 2 = 81.8%). Of the tear configurations, bucket handle tears were accurately identified (Accuracy observer 1 and 2 = 80%). The remaining tear configurations were not

accurately discernable.

CONCLUSION

Uni-planar 3D reconstruction from 3T MRI knee scan sequences are useful in identifying normal menisci and menisci with bucket-handle tears. Advances in MRI sequencing and reconstruction software are awaited for accurate identification of the remaining meniscal tear configurations.

Key words: Knee; Meniscus; Arthroscopy; Magnetic resonance imaging; Three-dimensional reconstruction; Materialise Interactive Medical Control System; Tear

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Three-dimensional reconstruction from magnetic resonance imaging (MRI) is an expanding field with potentially great clinical utility, but must be applied with caution when segmenting knee meniscal tears. Tear presence or absence, and the complex configuration of bucket handle tears were accurately distinguishable. The remaining tear configurations could not be correctly identified. Advances in MRI sequencing and reconstruction software need to be made before the remaining meniscal tear configurations will be identifiable.

Kruger N, McNally E, Al-Ali S, Rout R, Rees JL, Price AJ. Three-dimensional reconstructed magnetic resonance scans: Accuracy in identifying and defining knee meniscal tears. *World J Orthop* 2016; 7(11): 731-737 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/731.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.731>

INTRODUCTION

The knee menisci are vital to tibiofemoral contact mechanics^[1,2] and joint longevity^[3-5]. Tears thereof are common injuries^[6], occurring both as traumatic tears in younger patients and degenerate tears in older patients^[7,8]. Traumatic tears may adopt several different configurations^[9], depending predominantly upon the mechanism and extent of injury. By contrast, degenerate tears occur mainly as cleavage tears along the horizontal plane in which myxoid meniscal degeneration is known to occur^[10,11]. This variation in tear configuration and extent affects surgical planning regarding reparability or resection, and thus patient management. Accurate preoperative diagnosis is therefore important. Currently magnetic resonance imaging (MRI) is commonly used to preoperatively diagnose a meniscal tear. This however relies heavily on specialist radiological interpretation for diagnosis and adds further burden to a loaded service. Three-dimensional (3D) reconstruction from the MRI presents the data as a single alternative image for analysis. Interpretation of meniscal pathology in this

3D reconstructed meniscus is potentially simpler, as presentation of image data in three dimensions allows for better spatial relationship appreciation, easier object manipulation to view in any plane, and lessens the inferential burden on the observer.

3D meniscal reconstruction has accurately demonstrated meniscal dynamics relative to the tibial plateau^[12] and shown encouraging results in tear delineation, suggesting that 3D reconstruction may be particularly beneficial in showing up radial and horizontal tears not visible on the 2D MRI^[13]. Meniscal reconstruction has previously been used to investigate tibiofemoral contact^[14-16], and in calculating pre- and post-meniscectomy meniscal volumes^[17]. With current advancement in 3D reconstruction technology, this study aimed to determine whether 3D reconstruction of meniscal tears using current MRI protocols could accurately identify meniscal tears, and define their configuration.

MATERIALS AND METHODS

Study design

Cross sectional clinical cohort study.

Sample population

First the five common meniscal tear types were identified and categorised in groups as either radial, bucket handle (longitudinal displaced), parrot beak (oblique), cleavage (horizontal) and complex tears. Following, the operative notes of all arthroscopies undertaken on adult patients (aged over 18 years) by two experienced consultant orthopaedic surgeons at our institution were retrospectively reviewed to gather a minimum of five meniscal tears in each tear category. A further five normal menisci, defined at arthroscopy as having no tear or degeneration, were identified for each surgeon.

Subsequently the scans from these patients with the various tear configurations were retrieved for segmentation. In all cases arthroscopy was performed after preoperative MRI had indicated a potential meniscal tear. All preoperative scans were performed on a 3T MRI scanner (Philips) and reports on each by a subspecialized consultant musculoskeletal (MSK) radiologists were collected. Due to MRI data recording errors and one patient duplication, the final study population consisted of 24 meniscal tears in 24 patients, and nine control menisci.

MRI features

For all cases, imaging at 3T, and using a Philips Sense extremity Knee Coil, Fast Spin Echo (FSE) sequences were used to obtain Proton Density (PD) Fat Saturated images in the sagittal, coronal and axial planes. Following, a Gradient Recall Echo (GRE) sequence was employed to again image in the sagittal plane. The Time to Repetition (TR) varied from approximately 845 ms (for the GRE) to approximately 2500-7400 ms (for the PD). The Time to Echo (TE) varied from approximately 9 ms (for the GRE) to 30 ms (for the PD). The imaging characteristics were a Field of View (FOV) of 16 cm × 16 cm; a slice thickness of 2-3 mm; an

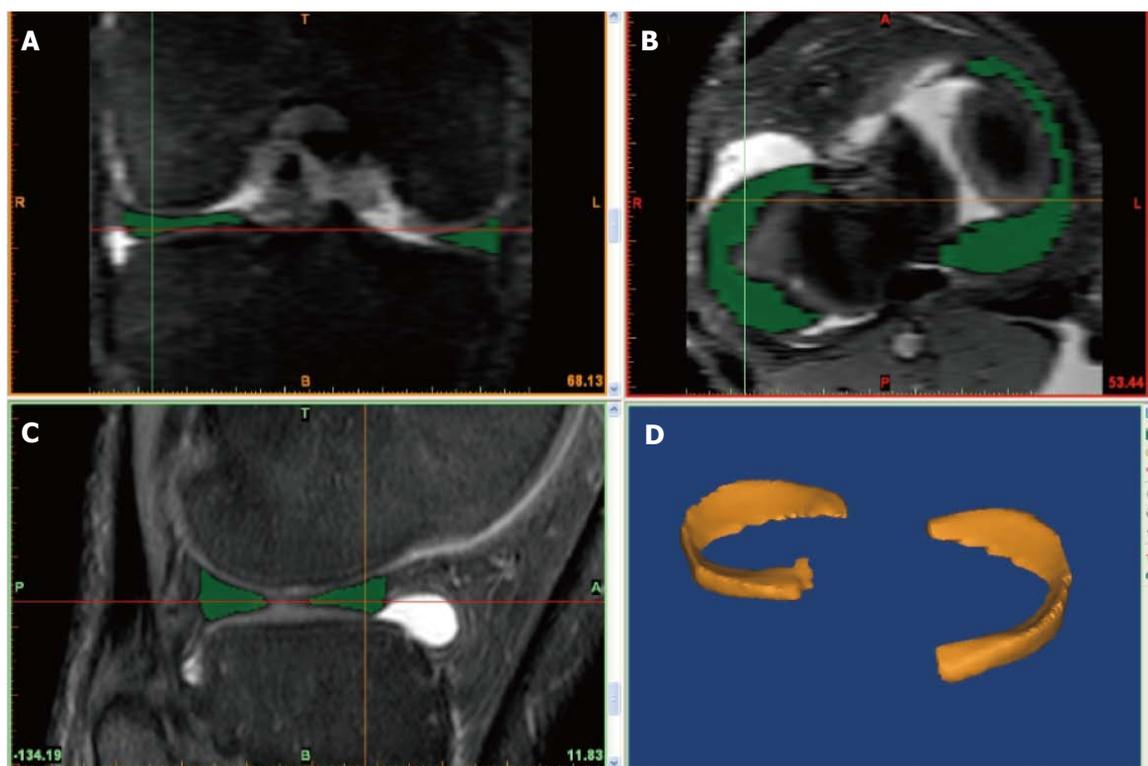


Figure 1 The user interface of the Materialise Interactive Medical Control System segmentation software program depicting the coronal view (A), the axial view (B), the sagittal view (C) and the three-dimensional reconstruction view (D). Note the poorer contrast and pixelated images in coronal and axial windows as compared the sagittal window.

interslice gap of between 2-3.3 mm; a matrix of either 512 × 512 or 1024 × 1024 and an Echo Train Length (ETL) of 14.

3D reconstruction

All patient MRI data for the 3T scans were imported into the Materialise Interactive Medical Control System (MIMICS) 3D reconstruction software program (Materialise, Leuven, Belgium) for subsequent reconstruction. All 33 scans were reconstructed from sagittal plane images by the lead author, segmenting both menisci for each knee scanned. This final image was then “wrapped” and stored as a finite element model for future interpretation. Each reconstruction was time consuming, taking approximately 4 h to generate the final model. In order to minimize the inaccuracies in the segmentation and reconstruction, the lead author undertook a two-day training course by the Materialise staff in using the novel software. Further, each reconstruction was reviewed for error in segmentation by a subspecialised MSK radiologist, and the adjacent uninjured meniscus reconstruction served as an innate control (Figure 1).

3D image analysis

Two orthopaedic trainees, who were both familiar with the different types of meniscal tears, reported on the reconstructions. Prior to reporting, each observer received a separate training session using this new software and were made familiar with user functions and object

manipulation, as well as normal and meniscal tear appearances in 3D. Each training session took no longer than ten minutes, as the user functions to zoom or pan and manipulate the image to view it in any desired plane are intuitive and easy to reproduce. There was hence no learning curve associated with this as the execution of each function is binary, and each surgeon was equipped with all the functions prior to undertaking the reporting.

Both trainees were blinded to the preoperative MRI and operative findings, and were blinded as to the number of tears in each configuration category. All 33 meniscal reconstructions were then brought up in random order in the MIMICS software program for independent reporting. Each observer prospectively reported their findings on a standard pro forma. Inter-observer and intra-observer repeatability were determined. Two primary assessments were made. First, tear presence vs absence was determined and subsequently the meniscal tear configuration was calculated (Figure 2).

RESULTS

Study population characteristics

Thirty-three patients were included in the final study, 20 were male and 13 were female. There were 14 tears in right knees and 10 tears in left knees. The 9 control patients consisted of 8 right knees and 1 left knee. Nineteen tears were in the medial meniscus and five tears were in the lateral meniscus. The mean time between

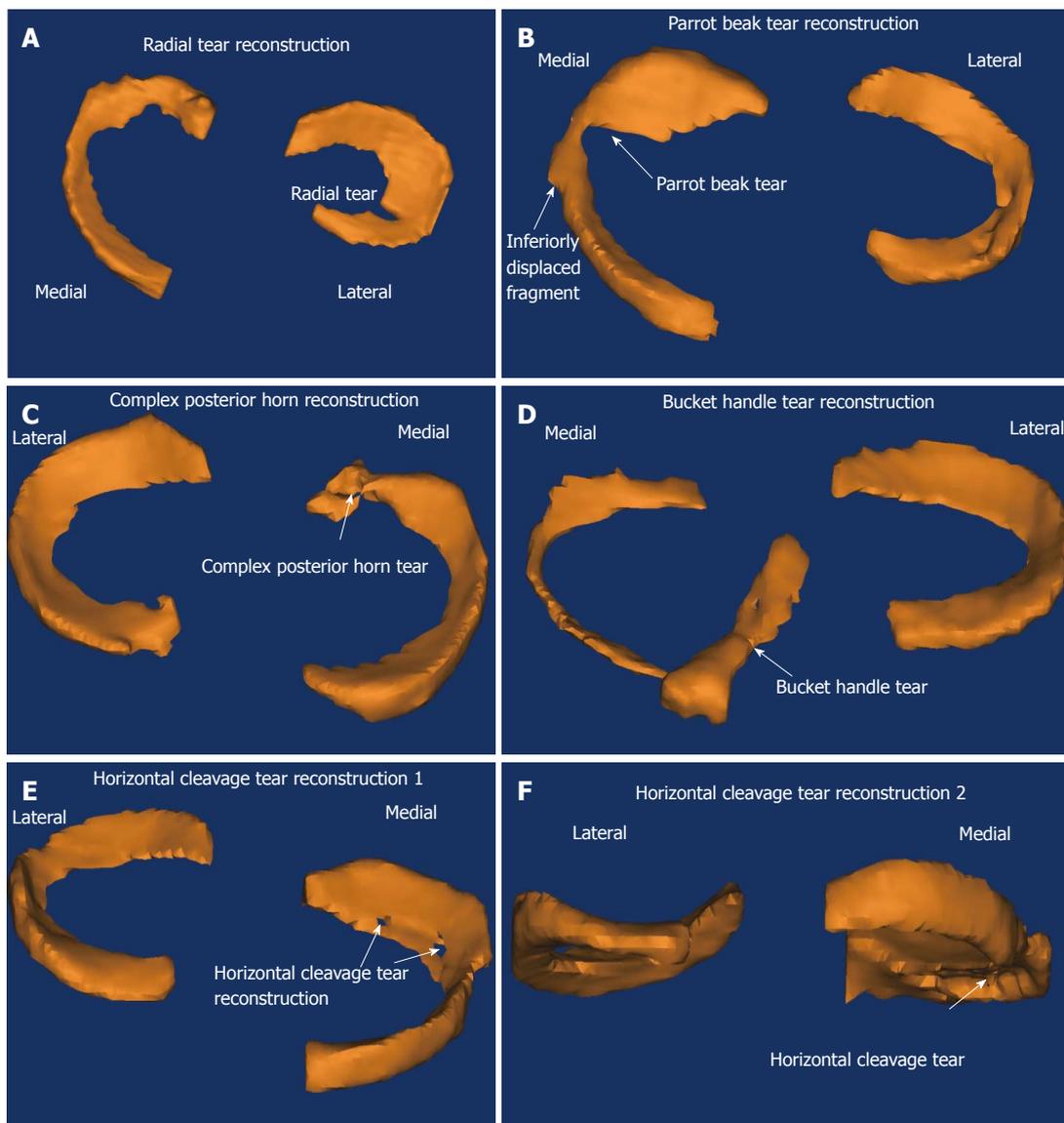


Figure 2 Three-dimensional reconstruction models showing an example of each configuration of meniscal tear identified in the study cohort. Note the two illustrations provided for the horizontal cleavage tear. A: Radial tear reconstruction; B: Parrot bile tear reconstruction; C: Complex posterior horn reconstruction; D: Bucket handle tear reconstruction; E: Horizontal cleavage tear reconstruction 1; F: Horizontal cleavage tear reconstruction 2.

MRI and arthroscopy was 4 mo (Range 1 mo to one year). All cases had arthroscopic validation of their tear configuration.

Results for all reconstructions

The accuracy and predicative values for detecting the presence or absence of a meniscal tear, regardless of tear configuration, were as follows.

Observer 1: The values for detecting tears presence vs absence were: Sensitivity 91.7%, specificity 88.9%, PPV 95.7%, NPV 80.0%, and accuracy 90.9%.

Observer 2: The values for detecting tears presence vs absence were: Sensitivity 87.5%, specificity 66.7%, PPV 87.5%, NPV 66.7%, and accuracy 81.8%. Both the intra- and inter-observer computed Cohen’s Kappa =

0.525, indicating a moderate degree of agreement.

Results for each meniscal tear configuration

Sub-classification for each tear configuration was then calculated for each observer: (1) Observer 1: Accuracy for detecting different tear configurations (Table 1); (2) Observer 2: Accuracy for detecting different tear configurations (Table 2).

As can be seen when comparing these results of the 3D reconstructions by meniscal tear configuration with those obtained on 2D MRI sequences from the literature in the table below, only the detection of bucket handle tears compares favourably (Table 3).

Morphological similarities

Morphological similarities, particularly in 3D reconstruction, between certain tear types exist. As evident from the

Table 1 Observer 1's meniscal tear configuration identification accuracy for all types of tear identified

Observer 1 tear configuration identification accuracy		
	Number of each tear correctly identified	Accuracy
Bucket handle	4 of 5	80%
Radial	1 of 6	16.7%
Cleavage	3 of 5	60%
Parrot beak	2 of 5	40%
Complex	1 of 3	33.3%

Table 2 Observer 2's meniscal tear configuration identification accuracy for all types of tear identified

Observer 2 tear type identification accuracy		
	Number of each tear correctly identified	Accuracy
Bucket handle	4 of 5	80%
Radial	3 of 6	50%
Cleavage	0 of 5	0%
Parrot beak	1 of 5	20%
Complex	2 of 3	66.7%

Table 3 The sensitivities for meniscal tear type detection for previous studies utilizing 2D magnetic resonance imaging as compared to the authors' results using the 3D reconstruction of meniscal tears

	Radial	Bucket-handle	Oblique	Horizontal cleavage	Complex
Jee <i>et al</i> ^[27]	8 of 11 (72.7%)	- ¹	3 of 5 (60.0%)	35 of 44 (79.5%)	18 of 22 (81.8%)
Jung <i>et al</i> ^[28]	26 of 36 (72.2%)	- ¹	2 of 2 (100.0%)	28 of 32 (87.5%)	1 of 2 (50.0%)
Wright <i>et al</i> ^[29]	- ¹	25 of 39 (64.1%)	- ¹	- ¹	- ¹
The present report	1 of 6 (16.7%)	4 of 5 (80.0%)	2 of 5 (40.0%)	3 of 5 (60.0%)	1 of 3 (33.3%)

¹No such tear configuration specified in the study.

reconstructions, the primary similarities are observed in the parrot beak and radial configurations, and the complex and cleavage tear configurations. Interestingly, when combining each into a single category, the sensitivities rivaled those of the normal and bucket handle tear configurations.

Observer 1: Accuracy when combining parrot beak and radial tears (7 of 11, 63.6%), and complex and cleavage tears (6 of 8, 75%).

Observer 2: Accuracy when combining parrot beak and radial tears (7 of 11, 63.6%), and complex and cleavage tears (7 of 8, 87.5%).

DISCUSSION

The MR diagnosis of a meniscal tear relies both on signal contrast and morphology. In un- or minimally displaced tears, the fluid entering the tear provides the contrasting signal with the surrounding normal meniscus, enabling the diagnosis. In severely displaced tears, the abnormal morphology of the meniscus is the key factor, indicating a tear is present. With 3D reconstruction from the MRI, these signal contrasts are utilised to provide distinct borders during the segmentation process to highlight out the meniscus, leaving only the morphology to interpret. Theoretically then, if the increased signal is seen on the 2D images, it should be reflected in the 3D reconstruction, enabling simpler diagnosis of tear presence and morphology.

In identifying meniscal tear presence or absence, the accuracies, sensitivities and specificities, as well as positive and negative predicative values in this study were equal to those obtained from 2D MRI^[18-20]. Advantages of the 3D reconstruction however include presenting the MRI data in

a visuospatially simple format and enabling object viewing in any plane to aid pathological identification. Further, it does not rely on radiologic skill or significant experience for interpretation.

Investigating by meniscal tear configuration, 3D reconstruction appeared useful in identifying normal menisci (Observer 1: Accuracy = 90.9%; Observer 2: Accuracy = 81.8%), and the complex configuration of bucket handle tears (Observer 1: Accuracy = 80.0%; Observer 2: Accuracy = 80.0%). However it had a lower accuracy in determining the remaining meniscal tear configurations.

Currently the achievement of adequate fine detail in 3D reconstruction enabling differentiation between morphologically similar tears is not possible using the present standard scan protocols. As can be seen when combining the morphologically similar tears above, the accuracy rivaled that achieved for the bucket handle tear configuration. Obscurements of meniscal tear border definition arise due to inaccuracies in the MRI, and in segmentation. MRI inaccuracies may be attributed to inherent magnetic field inhomogeneities, volume averaging and limited contrast dependent on the signal-to-noise ratio (SNR) maintainable across the FOV. Presently segmentation remains user dependent, time consuming and MRI quality reliant. Accurate tear and meniscal edge definition is still user defined, despite some semi-automated functions facilitating simpler and more efficient segmentation. While these inaccuracies are present, it is not possible to accurately determine meniscal tear extension to the periphery, this having clinical implication on prediction of healing whether or not the tear extends to the white-red zone or not.

Minimising these inaccuracies will increase the MRI quality, and hence the meniscal tear definition in 3D reconstruction. The greatest inaccuracy minimisation

would be achieved by eliminating the volume averaging occurring due to the interslice gaps in current clinical knee MRI sequences. Current clinical MRI knee scan protocols leads to three separate image series, only one of which may be imported and 3D reconstructed at a time. This leads to uni-planar reconstruction, as the interpolated images in the remaining two imaging planes are very pixelated and of poor quality.

Adopting an isotropic volume scan protocol for clinical knee MRI scanning eliminates the interslice gaps, as the whole volume is scanned simultaneously, producing true 3D MRI. Recently this has been investigated as an alternative to conventional knee scanning protocols, with comparable results^[21-25] obtained in a shorter scanning time^[26]. This has a great impact on 3D reconstruction, as the whole data volume is imported, resulting in equivalent contrast in all three-image window planes, allowing tri-planar 3D reconstructions. This tri-planar reconstruction is anticipated to have finer meniscal tear and border definition, increasing the accuracy in differentiating between the morphologically similar tears.

There are some limitations, both of the study and the practical applicability of the reconstructions, that merit discussion. The time consuming nature of the reconstructions mean that only a low number could be generated and this limits the robustness of the conclusions drawn. It also means that the real time clinical use of being able to present the 3D model on screen to the patient, however much it might aid understanding and appreciation of their pathology, is not presently possible.

The time between the MRI and arthroscopy was significant, and the potential for tear propagation or alteration of configuration exists. All patients however had arthroscopic corroboration of their MRI findings, so, for this patient cohort, there were no alterations in tear configurations, inaccurate tear assessment or false positive or negative diagnoses. Further, no differentiation between traumatic and degenerative tears was made. Although the pathophysiological processes that underpin these two tear types are distinct, as their diagnosis still relies on the separation of the tissue planes at the joint surface with synovial fluid entering the gap and altering the MR signal, this was deemed insignificant.

Lastly, longitudinal undisplaced tears were not included as one of the configurations for assessment, as the postulate was that being undisplaced, there would be too narrow a signal change for the 3D reconstruction to be able to accurately pick up the tear.

In conclusion, uni-planar 3D meniscal tear reconstruction is useful in identifying normal menisci and menisci with bucket handle tears. It however is unable to accurately report the remaining meniscal tear configurations. Significant technological advances need to be made in both MRI and 3D reconstruction, to rival 2D MRI diagnostic accuracy in defining meniscal tear configurations.

COMMENTS

Background

Three-dimensional (3D) imaging and reconstruction technology is becoming

more prevalent as an accepted imaging technique and, with respect to the knee meniscus, is attractive in presenting the whole meniscus on a single screen, with simple user functions enabling multiplanar visualization thereof. This technology has predominantly been applied to normal menisci in evaluation of knee kinematics and contact pressures during the gait cycle. However, meniscal tears adopt several different configurations and this abnormal morphology and signal generated on the magnetic resonance imaging (MRI) may complicate the reconstructions, thereby reducing the accuracy. This study aims to investigate whether 3D reconstruction from 2D MR images may presently be used to determine both the meniscal tear presence, and configuration.

Research frontiers

Presently the research emphasis on knee meniscus 3D reconstruction has been focused on generating models of the whole meniscus and its movement with respect to the tibial plateau during the gait cycle. This technology is being used extensively by the Osteoarthritis Initiative in the investigation of meniscal extrusion and its potential causation of osteoarthritis. No application to meniscal tear reconstruction is presently being undertaken.

Innovations and breakthroughs

To the authors' knowledge this is the first study to determine that 3D reconstruction from 2D MRI at present standard meniscal scan sequences is useful in determining normal menisci and menisci with bucket handle tears. It cautions the application to the remaining meniscal tear configurations.

Applications

Present application of the technology to practical diagnosis of a meniscal tear presence or absence appears possible and comparable to MRI. Similarly so in applying it bucket-handle tears, but not in the remaining meniscal tear configurations. Further technological development is needed in both the MRI and 3D reconstruction technology domains in order to improve the signal and contrast ratios, and the automation in tissue border definition to create the complete model respectively. Application of an isotropic voxel scan sequence and transition from 2D to 3D MRI in clinical imaging protocols to detect knee meniscal tears will go some way to improving this. Having the 3D reconstructed images of the meniscus at hand when consulting a patient also greatly aids understanding of their anatomy and hopefully soon, their pathology also.

Peer-review

The authors demonstrated the accuracy for meniscal tears on 3D reconstructed MRI. Uni-planar 3D meniscal tear reconstruction is useful in identifying normal menisci and menisci with bucket handle tears. It however is unable to accurately report the remaining meniscal tear configurations. The authors present an innovative technique in order to improve 3D reconstructed magnetic resonance scans: By adopting an isotropic volume scan protocol, the whole volume is scanned simultaneously enabling true tri-planar reconstruction. This is anticipated to have finer meniscal tear and border definition, increasing the accuracy in differentiating between the morphologically similar tears.

REFERENCES

- 1 **Masouros SD**, McDermott ID, Amis AA, Bull AM. Biomechanics of the meniscus-meniscal ligament construct of the knee. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 1121-1132 [PMID: 18802689 DOI: 10.1007/s00167-008-0616-9]
- 2 **Lee JM**, Allen CR, Fu, FH. Natural history of the post-meniscectomy knee. *Sports Med Arthroscopy Rev* 2002; **10**: 236-243 [DOI: 10.1097/00132585-200210040-00002]
- 3 **Ding C**, Martel-Pelletier J, Pelletier JP, Abram F, Raynauld JP, Cicuttini F, Jones G. Meniscal tear as an osteoarthritis risk factor in a largely non-osteoarthritic cohort: a cross-sectional study. *J Rheumatol* 2007; **34**: 776-784 [PMID: 17361984]
- 4 **Englund M**, Roos EM, Roos HP, Lohmander LS. Patient-relevant outcomes fourteen years after meniscectomy: influence of type of meniscal tear and size of resection. *Rheumatology (Oxford)* 2001; **40**: 631-639 [PMID: 11426019 DOI: 10.1093/rheumatology/40.6.631]
- 5 **Englund M**, Roos EM, Lohmander LS. Impact of type of meniscal

- tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. *Arthritis Rheum* 2003; **48**: 2178-2187 [PMID: 12905471 DOI: 10.1002/art.11088]
- 6 **Hede A**, Jensen DB, Blyme P, Sonne-Holm S. Epidemiology of meniscal lesions in the knee. 1,215 open operations in Copenhagen 1982-84. *Acta Orthop Scand* 1990; **61**: 435-437 [PMID: 2239168 DOI: 10.3109/17453679008993557]
 - 7 **Newman AP**, Daniels AU, Burks RT. Principles and decision making in meniscal surgery. *Arthroscopy* 1993; **9**: 33-51 [PMID: 8442828 DOI: 10.1016/S0749-8063(05)80342-1]
 - 8 **Hough AJ**, Webber RJ. Pathology of the meniscus. *Clin Orthop Relat Res* 1990; (252): 32-40 [PMID: 2406071 DOI: 10.1097/00003086-199003000-00005]
 - 9 **Boks SS**, Vroegindewij D, Koes BW, Hunink MM, Bierma-Zeinstra SM. Magnetic resonance imaging abnormalities in symptomatic and contralateral knees: prevalence and associations with traumatic history in general practice. *Am J Sports Med* 2006; **34**: 1984-1991 [PMID: 16861575 DOI: 10.1177/0363546506290189]
 - 10 **Stoller DW**, Martin C, Crues JV, Kaplan L, Mink JH. Meniscal tears: pathologic correlation with MR imaging. *Radiology* 1987; **163**: 731-735 [PMID: 3575724 DOI: 10.1148/radiology.163.3.3575724]
 - 11 **Jerosch J**, Castro WH, Assheuer J. Age-related magnetic resonance imaging morphology of the menisci in asymptomatic individuals. *Arch Orthop Trauma Surg* 1996; **115**: 199-202 [PMID: 8861590 DOI: 10.1007/BF00434553]
 - 12 **Thompson WO**, Thaete FL, Fu FH, Dye SF. Tibial meniscal dynamics using three-dimensional reconstruction of magnetic resonance images. *Am J Sports Med* 1991; **19**: 210-215; discussion 215-216 [PMID: 1867329 DOI: 10.1177/036354659101900302]
 - 13 **Disler DG**, Kattapuram SV, Chew FS, Rosenthal DI, Patel D. Meniscal tears of the knee: preliminary comparison of three-dimensional MR reconstruction with two-dimensional MR imaging and arthroscopy. *AJR Am J Roentgenol* 1993; **160**: 343-345 [PMID: 8424347 DOI: 10.2214/ajr.160.2.8424347]
 - 14 **Hao Z**, Jin D, Zhang Y, Zhang J. A finite element 3D model of in vivo human knee joint based on MRI for the tibiofemoral joint contact analysis. ICDHM'07 Proceedings of the First International Conference on Digital Human Modeling; 2007 July 22-27, Beijing, China. Berlin: Springer, 2007: 616-622
 - 15 **Zielinska B**, Donahue TL. 3D finite element model of meniscectomy: changes in joint contact behavior. *J Biomech Eng* 2006; **128**: 115-123 [PMID: 16532624 DOI: 10.1115/1.2132370]
 - 16 **DeFrate LE**, Sun H, Gill TJ, Rubash HE, Li G. In vivo tibiofemoral contact analysis using 3D MRI-based knee models. *J Biomech* 2004; **37**: 1499-1504 [PMID: 15336924 DOI: 10.1016/j.jbiomech.2004.01.012]
 - 17 **Bowers ME**, Tung GA, Fleming BC, Crisco JJ, Rey J. Quantification of meniscal volume by segmentation of 3T magnetic resonance images. *J Biomech* 2007; **40**: 2811-2815 [PMID: 17391677 DOI: 10.1016/j.jbiomech.2007.01.016]
 - 18 **Quinn SF**, Brown TR, Szumowski J. Menisci of the knee: radial MR imaging correlated with arthroscopy in 259 patients. *Radiology* 1992; **185**: 577-580 [PMID: 1410376 DOI: 10.1148/radiology.185.2.1410376]
 - 19 **Kojima KY**, Demlow TA, Szumowski J, Quinn SF. Coronal fat suppression fast spin echo images of the knee: evaluation of 202 patients with arthroscopic correlation. *Magn Reson Imaging* 1996; **14**: 1017-1022 [PMID: 9070992 DOI: 10.1016/S0730-725X(96)00144-0]
 - 20 **Cheung LP**, Li KC, Hollett MD, Bergman AG, Herfkens RJ. Meniscal tears of the knee: accuracy of detection with fast spin-echo MR imaging and arthroscopic correlation in 293 patients. *Radiology* 1997; **203**: 508-512 [PMID: 9114113 DOI: 10.1148/radiology.203.2.9114113]
 - 21 **Kijowski R**, Davis KW, Woods MA, Lindstrom MJ, De Smet AA, Gold GE, Busse RF. Knee joint: comprehensive assessment with 3D isotropic resolution fast spin-echo MR imaging--diagnostic performance compared with that of conventional MR imaging at 3.0 T. *Radiology* 2009; **252**: 486-495 [PMID: 19703886 DOI: 10.1148/radiol.2523090028]
 - 22 **Jung JY**, Yoon YC, Kwon JW, Ahn JH, Choe BK. Diagnosis of internal derangement of the knee at 3.0-T MR imaging: 3D isotropic intermediate-weighted versus 2D sequences. *Radiology* 2009; **253**: 780-787 [PMID: 19789228 DOI: 10.1148/radiol.2533090457]
 - 23 **Gold GE**, Busse RF, Beehler C, Han E, Brau AC, Beatty PJ, Beaulieu CF. Isotropic MRI of the knee with 3D fast spin-echo extended echo-train acquisition (XETA): initial experience. *AJR Am J Roentgenol* 2007; **188**: 1287-1293 [PMID: 17449772 DOI: 10.2214/AJR.06.1208]
 - 24 **Notohamiprodjo M**, Horng A, Pietschmann MF, Müller PE, Horger W, Park J, Crispin A, del Olmo JR, Weckbach S, Herrmann KA, Reiser MF, Glaser C. MRI of the knee at 3T: first clinical results with an isotropic PDfs-weighted 3D-TSE-sequence. *Invest Radiol* 2009; **44**: 585-597 [PMID: 19668001 DOI: 10.1097/RLI.0b013e3181b4c1a1]
 - 25 **Yao L**, Pitts JT, Thomasson D. Isotropic 3D fast spin-echo with proton-density-like contrast: a comprehensive approach to musculoskeletal MRI. *AJR Am J Roentgenol* 2007; **188**: W199-W201 [PMID: 17242228 DOI: 10.2214/AJR.06.0556]
 - 26 **Yoon YC**, Kim SS, Chung HW, Choe BK, Ahn JH. Diagnostic efficacy in knee MRI comparing conventional technique and multiplanar reconstruction with one-millimeter FSE PDW images. *Acta Radiol* 2007; **48**: 869-874 [PMID: 17924218 DOI: 10.1080/02841850701459791]
 - 27 **Jee WH**, McCauley TR, Kim JM, Jun DJ, Lee YJ, Choi BG, Choi KH. Meniscal tear configurations: categorization with MR imaging. *AJR Am J Roentgenol* 2003; **180**: 93-97 [PMID: 12490485 DOI: 10.2214/ajr.180.1.1800093]
 - 28 **Jung JY**, Jee WH, Park MY, Lee SY, Kim JM. Meniscal tear configurations: categorization with 3D isotropic turbo spin-echo MRI compared with conventional MRI at 3 T. *AJR Am J Roentgenol* 2012; **198**: W173-W180 [PMID: 22268208 DOI: 10.2214/AJR.11.6979]
 - 29 **Wright DH**, De Smet AA, Norris M. Bucket-handle tears of the medial and lateral menisci of the knee: value of MR imaging in detecting displaced fragments. *AJR Am J Roentgenol* 1995; **165**: 621-625 [PMID: 7645481 DOI: 10.2214/ajr.165.3.7645481]

P- Reviewer: Fernandez-Fairen M, Ohishi T, Papachristou GC
S- Editor: Kong JX **L- Editor:** A **E- Editor:** Lu YJ



Retrospective Cohort Study

Prosthetic design of reverse shoulder arthroplasty contributes to scapular notching and instability

Gazi Huri, Filippo Familiari, Nima Salari, Steve A Petersen, Mahmut Nedim Doral, Edward G McFarland

Gazi Huri, Mahmut Nedim Doral, Department of Orthopaedic and Traumatology Surgery, Hacettepe University Medical School, Ankara 06100, Turkey

Filippo Familiari, Nima Salari, Steve A Petersen, Edward G McFarland, Division of Shoulder Surgery, Department of Orthopaedic Surgery, the Johns Hopkins University, Baltimore, MD 21093, United States

Author contributions: Salari N and McFarland EG designed the research; Huri G, Familiari F and McFarland EG performed the research and analyzed the data; Huri G, Doral MN, Petersen SA and McFarland EG wrote the paper and critically revised the manuscript for important intellectual content.

Institutional review board statement: Institutional review board approval was obtained for this retrospective study.

Informed consent statement: Patients were not required to give the informed consent for the study.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest concerning this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Edward G McFarland, MD, Division of Shoulder Surgery, Department of Orthopaedic Surgery, The Johns Hopkins University, 10753 Falls Rd, Suite 215, Baltimore, MD 21093, United States. editorialservices@jhmi.edu
 Telephone: +1-410-5832850
 Fax: +1-410-5832855

Received: April 5, 2016

Peer-review started: April 13, 2016

First decision: May 19, 2016

Revised: July 14, 2016

Accepted: August 17, 2016

Article in press: August 18, 2016

Published online: November 18, 2016

Abstract

AIM

To evaluate whether implant design, glenoid positioning, and other factors influenced instability and scapular notching in reverse total shoulder arthroplasty.

METHODS

We retrospectively reviewed records of patients who had undergone reverse total shoulder arthroplasty by the senior author from July 2004 through October 2011 and who had at least 24 mo of follow-up. The 58 patients who met the criteria had 65 arthroplasties: 18 with a Grammont-type prosthesis (Grammont group) and 47 with a lateral-based prosthesis (lateral-design group). We compared the groups by rates of scapular notching and instability and by radiographic markers of glenoid position and tilt. We also compared glenoid sphere sizes and the number of subscapularis tendon repairs between the groups. Rates were compared using the Fisher exact test. Notching severity distribution was compared using the χ^2 test of association. Significance was set at $P < 0.05$.

RESULTS

The Grammont group had a higher incidence of scapular notching (13 of 18; 72%) than the lateral-design group (11 of 47; 23%) ($P < 0.001$) and a higher incidence of instability (3 of 18; 17%) than the lateral-design group (0 of 47; 0%) ($P = 0.019$). Glenoid position, glenoid sphere size, and subscapularis tendon repair were not predictive of scapular notching or instability, independent of implant

design. With the lateral-based prosthesis, each degree of inferior tilt of the baseplate was associated with a 7.3% reduction in the odds of developing notching (odds ratio 0.937, 95%CI: 0.894-0.983).

CONCLUSION

The lateral-based prosthesis was associated with less instability and notching compared with the Grammont-type prosthesis. Prosthesis design appears to be more important than glenoid positioning.

Key words: Arthroplasty; Reverse; Instability; Scapular notching; Shoulder

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: In reverse total shoulder arthroplasty (RTSA), we found that a Grammont-type prosthesis was associated with higher rates of instability and scapular notching and more severe notching compared with a prosthesis with a lateralized center of rotation. This study also suggests that some inferior tilt of the baseplate may decrease the notching rate. For the 2 prosthesis designs studied, neither glenoid sphere size nor repair of the subscapularis tendon was associated with rates of instability, rates of scapular notching, or severity of scapular notching. These findings are important to surgeons considering whether to use a Grammont-type prosthesis or a lateral-based implant when performing RTSA.

Huri G, Familiari F, Salari N, Petersen SA, Doral MN, McFarland EG. Prosthetic design of reverse shoulder arthroplasty contributes to scapular notching and instability. *World J Orthop* 2016; 7(11): 738-745 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/738.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.738>

INTRODUCTION

Since reverse total shoulder arthroplasty (RTSA) was approved by the United States Food and Drug Administration in December 2003 for the treatment of arthritis associated with rotator cuff disease, it has rapidly gained popularity for treating patients with various shoulder conditions, including rotator cuff tear arthropathy, degenerative arthritis with rotator cuff deficiency, and pseudoparalysis associated with anterosuperior escape syndrome. Although RTSA provides pain relief in most patients, its associated rate and variety of complications are higher than those for anatomical total shoulder arthroplasty^[1,2].

There are 2 designs of reverse total shoulder prosthesis. One is a Grammont-type prosthesis, which has a center of rotation at the level of the glenoid where the baseplate meets the bone^[1]. The other, available from various manufacturers, has a center of rotation in a more lateral position, which theoretically increases the shear

forces across the baseplate-to-glenoid bone interface^[3].

The most common complications of RTSA are instability and scapular notching. Reported rates of instability range from 0%-31%^[4-9]. Instability has been associated with component malposition^[10], inadequate tensioning of the soft-tissue envelope^[11-13], insufficient subscapularis tendon for repair^[14], and use of the deltopectoral approach vs the superolateral approach^[11,15]. Scapular notching is a concern because of its potential effect on long-term loosening of the prosthesis and on clinical results^[16]. Reported rates of inferior scapular notching for a Grammont-type prosthesis range from 13%-67%^[12,15-18].

Studies have compared the severity of scapular notching associated with different RTSA designs^[19,20]. However, these studies included patients with a variety of diagnoses, as well as patients who underwent revision arthroplasty, which is associated with higher complication rates than primary RTSA^[19,20]. They also included patients with a minimum follow-up of only 12 mo^[19,20]. Although these studies addressed notching associated with RTSA, they did not address instability factors that might also be related to prosthesis positioning and design^[18,20].

In patients with rotator cuff tear arthropathy, osteoarthritis with a rotator cuff tear, or osteoarthritis with glenoid bone loss, we sought to: (1) establish and compare the instability rates of those treated with a Grammont-type prosthesis vs a lateral-based prosthesis; (2) establish and compare the rates and severity of scapular notching between the 2 groups; and (3) determine in both groups whether glenoid baseplate position, repair of the subscapularis tendon, and glenoid sphere size were associated with different rates and severity of scapular notching.

MATERIALS AND METHODS

Institutional review board approval was obtained for this retrospective study.

Study population

From July 2004 through October 2011, 324 RTSAs were performed by the senior author, 196 of which had at least 2 years of follow-up. We included only patients undergoing their first RTSA with the diagnosis of rotator cuff tear arthropathy, osteoarthritis with a rotator cuff tear, or osteoarthritis with glenoid bone loss. Of those 196 RTSAs, 131 were excluded for the following reasons: 57 that were revised with a diagnosis of failed arthroplasty (based on clinical history, physical examination, and supporting radiographic studies); 37 for fractures and malunion; 17 for rheumatoid arthritis; 7 for inadequate follow-up data; 5 for avascular necrosis; 5 for dislocation arthroplasty; 2 for psoriatic arthritis; and 1 for hemophilic arthropathy. Therefore, our study group comprised 65 shoulders in 58 consecutive patients with a mean follow-up of 35 mo (range, 24-66 mo). Patients had surgery at a mean age of 70 ± 8.1 years. According to the glenoid

Table 1 Characteristics of 58 adults who underwent 65 reverse total shoulder arthroplasties, 2004-2011

Characteristic	Grammont group (n = 18)		Lateral-design group (n = 47)		P-value
	Mean ± SD	n (%)	Mean ± SD	n (%)	
Male sex		12 ¹ (67)		31 ¹ (66)	NA ¹
Age (yr)	69 ± 7.3		70 ± 8.4		0.722
Follow-up (mo)	43 ± 15		32 ± 7.9		0.0004
Dominant side affected		12 (67)		2 ¹ (45)	NA
Workers compensation		0 ² (0)		2 ² (3.4)	NA
Glenoid sphere diameter					
32 mm		0 ¹ (0)		28 (60)	NA
≥ 36 mm		18 ¹ (100)		19 (40)	NA

¹Number of shoulders; ²Number of patients. NA: Not applicable; SD: Standard deviation.

bone loss classification system of Walch *et al*^[21], there were 27 A2 glenoids, 15 B1 glenoids, 10 B2 glenoids, and 13 C glenoids.

From 2004 to 2007, we used a Grammont-type prosthesis (Tornier Inc., Stafford, Texas, United States) (the Grammont group, n = 18), and from 2007 to 2011 we used a prosthesis with a lateral-based center of rotation (DJO/Encore Medical Corporation, Austin, Texas, United States) (the lateral-design group, n = 47) (Table 1). There was no significant difference in mean age between groups (P = 0.722), but there was a significant difference in mean length of follow-up was longer in the Grammont group (P = 0.0004).

Surgical and postoperative details

Surgery was performed with patients in a beach chair position. All patients received general anesthesia with a scalene block or indwelling scalene catheter, as well as perioperative antibiotics. All surgical procedures were performed with a deltopectoral approach.

The glenoid was exposed circumferentially, and the glenoid component position was determined with guides provided by the prosthesis manufacturer. An attempt was made to place the glenoid component in approximately 10° of inferior inclination, but this was done visually with no measurement. The size of the glenoid sphere was chosen to best fit the glenoid size and the soft-tissue tension in each patient. In the Grammont group, the glenoid sphere diameters were 36 mm in 16 shoulders, 38 mm in 1 shoulder, and 42 mm in 1 shoulder. In the lateral-design group, the glenoid sphere diameters were 32 mm in 28 shoulders and 36 mm in 19 shoulders. In all patients, regardless of implant type, the humeral components were inserted in 30° of retroversion, and all components were cemented. Stability of the implants after reduction of the humeral component on the sphere was verified by moving the arm in rotation and also with axial distraction. The subscapularis tendon or anterior capsule was secured back to the proximal humerus when possible [in 9 (50%) of 18 shoulders in the Grammont group and 39 (83%) of 47 shoulders in the lateral-design group]. A biceps tenodesis was performed in all shoulders in which the biceps tendon was present.

After surgery, each shoulder was placed in an

immobilizer. Unlimited motion was allowed in elevation and internal rotation, but external rotation was limited for 6 wk. Patients were not allowed to lift more than 0.45 kg for 3 mo. No patient had a structured rehabilitation program, but all were encouraged to use the arm for activities of daily living. Radiographs were obtained every 3 mo for the first year and then yearly.

At each follow-up evaluation, 3 conventional radiographs were obtained (a true anteroposterior view in external rotation (Grashey view)^[22], an anteroposterior view in internal rotation, and an axillary view). Fluoroscopy was not used for any radiographs.

The presence of notching was evaluated by 2 observers who reached agreement upon the degree of notching using the system of Sirveaux *et al*^[15]. Grade 1 was notching limited to the scapular pillar; grade 2 was notching in contact with the inferior screw of the baseplate; grade 3 was notching beyond the inferior screw; and grade 4 was notching that extends under the baseplate approaching the central peg.

Evaluation

Instability was determined using clinical examination and radiographic evidence of component dislocation. Radiographic analysis was performed by an independent observer. Scapular notching was graded according to the 4-grade classification system of Sirveaux *et al*^[15] (Figure 1). The vertical position of the glenoid sphere was evaluated using 2 similar methods. First, using a method proposed by Lévine *et al*^[23], we measured the distance between the inferior glenoid osseous rim and the lowest point of the glenoid sphere on the external rotation anteroposterior view (Figure 2). Second, as proposed by Simovitch *et al*^[16], we measured the peg-glenoid rim distance on the same view using a point marking the radiographic superior intersection of the central peg (or central screw in the lateral-based implant) and the glenoid sphere, and a point referencing the most inferior bone of the inferior glenoid rim adjacent to the medial surface of the glenoid sphere (Figure 3).

The inclination of the glenoid sphere was measured in 3 ways. The first method, described by Levigne *et al*^[23], uses a horizontal line placed on the most superior aspect of the glenoid on the anteroposterior radiograph.

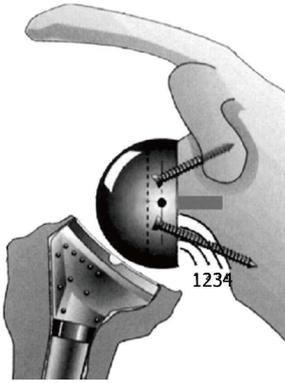


Figure 1 Scapular notching according to the 4-grade Sirveaux classification. Reproduced with permission and copyright of the British Editorial Society of Bone and Joint Surgery (Reprinted with permission from Sirveaux F *et al*^[15], Figure 3).

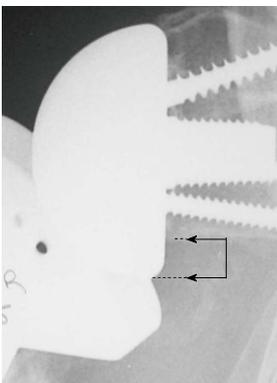


Figure 2 Distance between the inferior glenoid osseous rim (upper arm of the arrow) and the lowest point of the glenoid sphere (lower arm of the arrow) on the external rotation anteroposterior view. Reprinted with permission from Levigne C *et al*^[23], Figure 8.

The angle formed between the horizontal line and a line parallel to the back surface of the glenoid sphere is measured; if it is $> 90^\circ$, it is considered superiorly tilted, and if it is $\leq 90^\circ$, it is considered inferiorly tilted (Figure 4). The second method, described by Simovitch *et al*^[16], defines the prosthesis-scapular neck angle as the angle between a line from superior to inferior along the glenoid baseplate and a line from the most inferior point of the baseplate's prosthesis-bone interface to a point 1 cm medially along the inferior scapular neck (Figures 3 and 5A). The third method was described by Kempton *et al*^[24], who noted that scapular neck anatomy can be highly variable at 1 cm from the baseplate and may be altered by eccentric reaming or previous surgery. Therefore, they defined a point 6 cm medial along the scapular border to which one draws the second line, which defines the prosthesis-scapular bone angle (Figure 5B).

Statistical analysis

To determine the association of prosthesis design with instability, we used a stepwise logistic regression model that included inferior glenoid notching, glenoid position^[23], glenoid inclination^[23], peg-glenoid rim distance^[16],

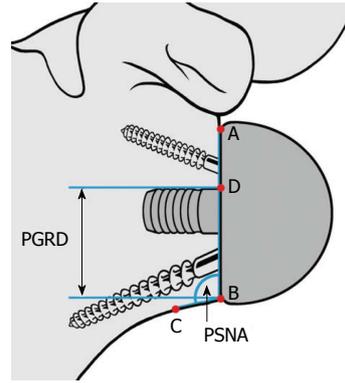


Figure 3 The prosthesis-scapular neck angle (PSNA) is the angle subtended by the intersection of line AB and line BC. Point C is located 1 cm medial to the junction of the glenosphere and the most inferior and lateral bone of the inferior glenoid rim or scapular neck. The peg-glenoid rim distance (PGRD) is the distance between points B and D.. PGRD: Peg-glenoid rim distance; PSNA: Prosthesis-scapular neck angle. Reprinted with permission from Simovitch *et al*^[16], Figure 4A.



Figure 4 Glenoid inclination is the angle formed between a horizontal line and a line parallel to the back surface of the glenoid sphere. If it is $> 90^\circ$ it is classified as superiorly tilted, and if it is $\leq 90^\circ$ it is classified as inferiorly tilted. Reprinted with permission from Levigne *et al*^[23], Figure 11.

prosthesis-scapular neck angle^[24], and prosthesis-scapular bone angle^[24]. Variable selection was made on the basis of a forward stepwise selection method, with marginal significance levels set at 5% for entry and 10% for removal. This approach to model building was selected to minimize collinearity (redundancy) among variables^[25].

We calculated the likelihood of instability as a function of subscapularis repair, glenoid sphere diameter, and inferior inclination using logistic regression within each prosthetic group and in the overall cohort. Receiver operating characteristic (ROC) curves were used to determine the optimal inferior tilt according to presence of instability and scapular notching. ROC curves plot sensitivity vs 1 - specificity to determine the discrimination threshold.

Rates between design groups were compared using the Fisher exact test. Distribution of notching type was compared between design groups using the χ^2 test of association. Statistical analysis was performed using SAS, version 9.3, software (SAS Institute, Cary,

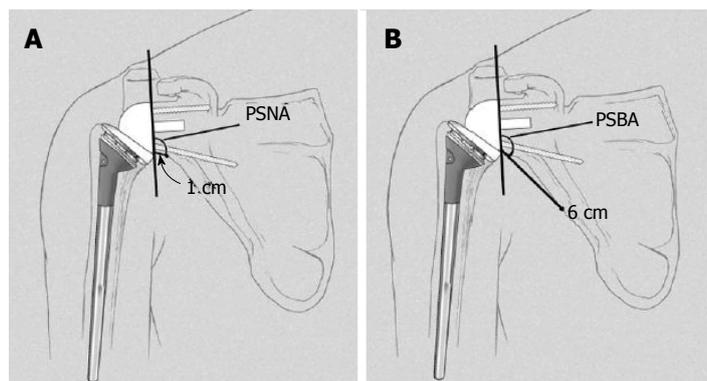


Figure 5 Illustration of measurement of the prosthesis-scapular neck angle and the prosthesis-scapular bone angle. A: The prosthesis-scapular neck angle is the angle between a line from superior to inferior along the glenoid baseplate and a line from the most inferior point of the baseplate's prosthesis-bone interface to a point 1 cm medially along the inferior scapular neck; B: The prosthesis-scapular bone angle uses a point 6 cm medial along the scapular border to draw the second line. PSNA: Prosthesis-scapular neck angle; PSBA: Prosthesis-scapular bone angle. Reprinted with permission from Kempton *et al*^[24], Figure 3.

Table 2 Scapular notching and instability by prosthesis design in 65 cases of reverse total shoulder arthroplasty with minimum 2-year follow-up, 2004-2011¹

Parameter	Grammont group (n = 18), n (%)	Lateral-design group (n = 47), n (%)	P-value
Scapular notching	13 (72)	11 (23)	< 0.001 ²
Notching severity ³			
Grade 1	7 (39)	8 (17)	> 0.001 ³
Grade 2	2 (11)	1 (2.1)	NA ⁴
Grade 3	2 (11)	2 (4.3)	NA ⁴
Grade 4	2 (11)	0 (0)	NA ⁴
Instability ⁶	3 (17)	0 (0)	0.019

¹NA: Not applicable; ²P-value from two-tailed Fisher exact test; ³Adjusted for length of follow-up using general linear model; ⁴Small values prevented determination of significant differences; ⁵Notching severity was measured according to Sirveaux classification^[15]; ⁶Instability was determined using clinical examination and radiographic evidence of component dislocation.

North Carolina, United States) and SPSS, version 20.0, software (SPSS, Chicago, IL, United States). Statistical significance was set at $P < 0.05$.

An individual with advanced training in biostatistics was involved in the design or analysis of this work. No additional data are available.

RESULTS

There were 3 dislocations in the Grammont group and none in the lateral-design group, which was a significant difference ($P = 0.014$). There was a significantly higher rate of subscapularis tendon repair in the lateral-design group ($P = 0.008$). However, there was no association between dislocation and the presence of a subscapularis repair in either group ($P = 0.170$). Smaller glenoid spheres were used in the lateral-design group compared with the Grammont group ($P < 0.001$).

The rate of scapular notching was significantly higher in the Grammont group (13 of 18 shoulders, 72%) than in the lateral-design group (11 of 47 shoulders; 23%) ($P < 0.001$) (Table 2). Patients in the Grammont group had higher odds of developing notching [odds ratio (OR), 7.2; 95%CI: 2.1-24.7] and had significantly more severe notching than patients in the lateral-design group ($P = 0.003$). This association between the rate and severity of notching between the 2 implant systems persisted even after adjustment for length of follow-up using a general linear model ($P = 0.001$).

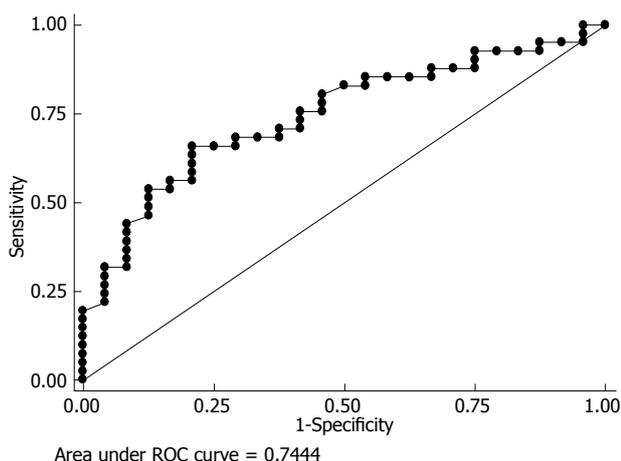
According to the method of Levigne *et al*^[23] there were significant differences in glenoid position between the lateral-design group and the Grammont group ($P = 0.004$). There was significantly more glenoid inclination in the lateral-design group than the Grammont group ($P = 0.027$). However, there were no significant differences between the 2 groups for prosthesis-scapular neck angle ($P = 0.368$), prosthesis-scapular bone angle ($P = 0.219$), or peg-glenoid rim distance ($P = 0.066$) (Table 3).

We found no factors to be significantly associated with glenoid notching in the Grammont group. However, in the lateral-design group, glenoid inclination, prosthesis-scapular bone angle, and peg-glenoid rim distance were associated with the rate of notching. In the lateral-design group, for each 1° increase in the angle of glenoid inclination, there was a 7.3% reduction in the odds of developing notching (OR, 0.94; 95%CI: 0.89-0.98); for each 1° increase in the prosthesis-scapular bone angle, there was a 9.7% reduction in the odds of developing notching (OR, 0.09; 95%CI: 0.83-0.98); and for each 1-mm increase in the peg-glenoid rim distance, there was a 34% increase in the odds of developing notching (OR, 1.3; 95%CI: 1.0-1.7). A ROC curve analysis revealed that a glenoid inclination angle of $< 99.8^\circ$ tends to be associated with more notching than an angle of $\geq 99.8^\circ$ (sensitivity, 66%; specificity, 75%).

Using ordinal logistic regression, we found that as the glenoid inclination angle increased in the lateral-

Table 3 Glenoid position by prosthesis design in 65 cases of reverse total shoulder arthroplasty, 2004-2011

Parameter	Grammont group (<i>n</i> = 18), mean ± SD	Lateral-design group (<i>n</i> = 47), mean ± SD	<i>P</i> -value
Glenoid position (mm)			
Inferior glenoid osseous rim to lowest point of glenoid sphere ^[23]	1.5 ± 2.1	-0.6 ± 3.3	0.004
Peg-glenoid rim distance ^[16]	22.6 ± 1.7	21.4 ± 3.3	0.066
Glenoid inclination (°)			
Inclination angle ^[23]	93.2 ± 15.3	101 ± 11.7	0.027
Prosthesis-scapular neck angle ^[16]	102 ± 21.3	106 ± 17.1	0.368
Prosthesis-scapular bone angle ^[24]	126 ± 16.9	132 ± 11.0	0.219

**Figure 6** The receiver operating characteristic curve reveals the sensitivity and specificity for predicting the inferior glenoid tilt.

based prosthesis, the likelihood of more severe scapular notching decreased (OR, 0.95; 95%CI: 0.91-0.98).

Based on the ROC curve, an inferior tilt of < 100.5° maximizes the sensitivity (66%) and specificity (79%) of discriminating between shoulders that develop scapular notching and those that do not (area under the curve, 0.74; 95%CI: 0.62-0.87) (Figure 6).

DISCUSSION

We sought to determine whether the design of the RTSA prosthesis and other factors such as subscapularis tendon repair, glenoid positioning, and glenoid sphere size were associated with differences in the rate of prosthesis instability, the rate of scapular notching, and the severity of scapular notching. We found that implant design was a significant factor in the development of instability, the rate of notching, and the severity of notching. Subscapularis repair and glenoid sphere size were not associated with differences in instability rates for either prosthesis design. The baseplate in the lateral-based prosthesis should be placed with some inferior tilt, and a more inferior baseplate position is associated with lower rates of scapular notching.

We observed a 4.5% instability rate (all occurrences in the Grammont group), which is similar to those of previous reports (2.4%-31%)^[4,5,7]. However, those studies included revision cases and a wider range of

preoperative diagnoses^[4,5,7]. Glenoid sphere size and offsets in designs other than the Grammont-type prosthesis may play a crucial role in prosthesis stability; it has been postulated that proper glenoid sphere offset allows the deltoid to provide a compressive force that keeps the ball pressed into the socket^[26]. Subsequent prosthetic designs have created offset by increasing the diameter of the glenoid sphere, placing a humeral neck extension beneath the polyethylene cup, and/or increasing the thickness of the polyethylene cup^[27]. Our study supports the observation of Clark *et al*^[28], who found that repair of the subscapularis tendon does not influence dislocation rates of the Grammont-type prosthesis.

We observed a 72% rate of scapular notching in the Grammont group, which is similar to those reported in the literature (range, 13%-67%)^[12,15-17]. However, we found a 23% rate of scapular notching in the lateral-design group, which is higher than those reported in the literature (range, 0%-13%)^[6,26,29]. Two factors have been suggested for the lower rates of notching in the lateral-based prosthesis: (1) the design of the glenoid side of the prosthesis; and (2) the humeral head-neck angle. Until a reverse prosthesis is developed that allows surgeons to choose between a lower or higher humeral head-neck angle, it is unlikely that we will know which factor is responsible for lower rates of notching.

Several studies have suggested that prosthesis design and baseplate and glenoid sphere position may influence scapular notching rates^[19,20,30]. Our study is consistent with that of Gutiérrez *et al*^[31], who found in a biomechanical model that tilting the glenoid component inferiorly might prevent notching by decreasing contact of the humeral component to the scapula. We found that glenoid tilt of < 100° was associated with more, and more severe, notching. We also found that inferior placement of the baseplate was associated with less notching for the lateral-based prosthesis, similar to the findings of Simovitch *et al*^[16]. Berhouet *et al*^[32] found the most effective way to prevent scapular notching was by using large-diameter glenoid spheres, but our study did not support that finding.

Our study had several limitations. It was neither prospective nor randomized, and because it was a consecutive series, the mean length of follow-up differed between the 2 groups. The rate and severity of notching

in the lateral-design group might have been higher had the follow-up been longer. There were fewer shoulders in the Grammont group than in the lateral-design group, making type-2 error possible. We limited our study to patients undergoing primary RTSA for rotator cuff tear arthropathy, osteoarthritis with a rotator cuff tear, or osteoarthritis with glenoid bone loss. Therefore, our results may not be generalizable to RTSA for other causes or for revisions. It is possible that another design feature—the humeral head-neck angle—is partly responsible for our results. The humeral head-neck angle is 135° in the Grammont-type prosthesis and 155° in the lateral-based prosthesis. It was impossible for us to determine whether the humeral head-neck angle or the location of the center of rotation was the most important factor in our results. In addition, we evaluated only 2 implant systems, so our results may not apply to other systems. Also, variables not studied here such as body mass index, Charlson Comorbidity Index, or other measures of patient health might influence the results.

The surgery was performed by 1 surgeon in a referral practice, which may not be generalizable to other surgical practices. Also, the surgeon changed arthroplasty systems, and the learning curve might have affected the results. Wierks *et al.*^[33] suggested that the learning curve for a new operation is approximately 10 cases, but Kempton *et al.*^[34] suggested it might be as high as 40 cases.

Another limitation is that we used standard radiographs not obtained with fluoroscopy. The routine use of fluoroscopy for shoulder radiography has not been the practice at our institution for ethical and financial reasons. Several radiographic measures are described in the literature to assess glenoid position and tilt, but their relation to scapular notching has not been thoroughly studied^[16,23,24]. To our knowledge, ours is the first study to correlate the peg-glenoid rim distance and the prosthesis-scapular neck angle with the rate of inferior scapular notching between the Grammont-type prosthesis and the lateral-based prosthesis. Furthermore, unlike previous reports^[16], we found no single statistically significant radiographic factor related to glenoid notching in the Grammont group.

In conclusion, we found the Grammont-type of RTSA was associated with significantly higher rates of instability and scapular notching, as well as more severe scapular notching compared with a prosthesis with a lateralized glenoid sphere center of rotation and a decreased humeral head-neck angle. These findings are important to the surgeon when considering whether to use a Grammont-type prosthesis or a lateral-based implant when performing RTSA. This study also suggests that some inferior tilt of the baseplate may decrease the scapular notching rate and that, for the 2 prosthesis designs studied, neither glenoid sphere size nor repair of the subscapularis tendon was associated with different rates of instability, rates of scapular notching, or severity of scapular notching.

COMMENTS

Background

Since reverse total shoulder arthroplasty (RTSA) was approved by the United States Food and Drug Administration in December 2003 for the treatment of arthritis associated with rotator cuff disease, it has rapidly gained popularity for treating patients with various shoulder conditions, including rotator cuff tear arthropathy, degenerative arthritis with rotator cuff deficiency, and pseudoparalysis associated with anterosuperior escape syndrome.

Research frontiers

Although RTSA provides pain relief in most patients, its associated rate and variety of complications are higher than those for anatomical total shoulder arthroplasty.

Innovations and breakthroughs

The authors found the Grammont-type of RTSA was associated with significantly higher rates of instability and scapular notching, as well as more severe scapular notching compared with a prosthesis with a lateralized glenoid sphere center of rotation and a decreased humeral head-neck angle.

Applications

The findings are important to the surgeon when considering whether to use a Grammont-type prosthesis or a lateral-based implant when performing RTSA. This study also suggests that some inferior tilt of the baseplate may decrease the scapular notching rate and that, for the 2 prosthesis designs studied, neither glenoid sphere size nor repair of the subscapularis tendon was associated with different rates of instability, rates of scapular notching, or severity of scapular notching.

Peer-review

As a retrospective cohort study, this is low level evidence. However, it does provide clinically relevant information for surgeons who perform RTSA surgery and is worthy of publication.

REFERENCES

- 1 **Grammont PM**, Baulot E. Delta shoulder prosthesis for rotator cuff rupture. *Orthopedics* 1993; **16**: 65-68 [PMID: 8421661]
- 2 **Scariat MM**. Complications with reverse total shoulder arthroplasty and recent evolutions. *Int Orthop* 2013; **37**: 843-851 [PMID: 23456086 DOI: 10.1007/s00264-013-1832-6]
- 3 **Henninger HB**, Barg A, Anderson AE, Bachus KN, Burks RT, Tashjian RZ. Effect of lateral offset center of rotation in reverse total shoulder arthroplasty: a biomechanical study. *J Shoulder Elbow Surg* 2012; **21**: 1128-1135 [PMID: 22036546 DOI: 10.1016/j.jse.2011.07.034]
- 4 **Cazeneuve JF**, Cristofari DJ. The reverse shoulder prosthesis in the treatment of fractures of the proximal humerus in the elderly. *J Bone Joint Surg Br* 2010; **92**: 535-539 [PMID: 20357330 DOI: 10.1302/0301-620x.92b4.22450]
- 5 **Cheung E**, Willis M, Walker M, Clark R, Frankle MA. Complications in reverse total shoulder arthroplasty. *J Am Acad Orthop Surg* 2011; **19**: 439-449 [PMID: 21724923 DOI: 10.5435/0124635-201107000-00007]
- 6 **Cuff D**, Pupello D, Virani N, Levy J, Frankle M. Reverse shoulder arthroplasty for the treatment of rotator cuff deficiency. *J Bone Joint Surg Am* 2008; **90**: 1244-1251 [PMID: 18519317 DOI: 10.2106/JBJS.G.00775]
- 7 **Gerber C**, Pennington SD, Nyffeler RW. Reverse total shoulder arthroplasty. *J Am Acad Orthop Surg* 2009; **17**: 284-295 [PMID: 19411640 DOI: 10.5435/00124635-200905000-00003]
- 8 **Guery J**, Favard L, Sirveaux F, Oudet D, Mole D, Walch G. Reverse total shoulder arthroplasty. Survivorship analysis of eighty replacements followed for five to ten years. *J Bone Joint Surg Am* 2006; **88**: 1742-1747 [PMID: 16882896 DOI: 10.2106/JBJS.E.00851]
- 9 **Wall B**, Nové-Josserand L, O'Connor DP, Edwards TB, Walch G.

- Reverse total shoulder arthroplasty: a review of results according to etiology. *J Bone Joint Surg Am* 2007; **89**: 1476-1485 [PMID: 17606786 DOI: 10.2106/JBJS.F.00666]
- 10 **Stephenson DR**, Oh JH, McGarry MH, Rick Hatch GF, Lee TQ. Effect of humeral component version on impingement in reverse total shoulder arthroplasty. *J Shoulder Elbow Surg* 2011; **20**: 652-658 [PMID: 21144775 DOI: 10.1016/j.jse.2010.08.020]
 - 11 **Affonso J**, Nicholson GP, Frankle MA, Walch G, Gerber C, Garzon-Muvdi J, McFarland EG. Complications of the reverse prosthesis: prevention and treatment. *Instr Course Lect* 2012; **61**: 157-168 [PMID: 22301230]
 - 12 **Boileau P**, Watkinson DJ, Hatzidakis AM, Balg F. Grammont reverse prosthesis: design, rationale, and biomechanics. *J Shoulder Elbow Surg* 2005; **14**: 147S-161S [PMID: 15726075 DOI: 10.1016/j.jse.2004.10.006]
 - 13 **Gallo RA**, Gamradt SC, Mattern CJ, Cordasco FA, Craig EV, Dines DM, Warren RF. Instability after reverse total shoulder replacement. *J Shoulder Elbow Surg* 2011; **20**: 584-590 [PMID: 21167744 DOI: 10.1016/j.jse.2010.08.028]
 - 14 **Edwards TB**, Williams MD, Labriola JE, Elkousy HA, Gartsman GM, O'Connor DP. Subscapularis insufficiency and the risk of shoulder dislocation after reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2009; **18**: 892-896 [PMID: 19282204 DOI: 10.1016/j.jse.2008.12.013]
 - 15 **Sirveaux F**, Favard L, Oudet D, Huquet D, Walch G, Molé D. Grammont inverted total shoulder arthroplasty in the treatment of glenohumeral osteoarthritis with massive rupture of the cuff. Results of a multicentre study of 80 shoulders. *J Bone Joint Surg Br* 2004; **86**: 388-395 [PMID: 15125127 DOI: 10.1302/0301-620X.86B3]
 - 16 **Simovitch RW**, Zumstein MA, Lohri E, Helmy N, Gerber C. Predictors of scapular notching in patients managed with the Delta III reverse total shoulder replacement. *J Bone Joint Surg Am* 2007; **89**: 588-600 [PMID: 17332108 DOI: 10.2106/JBJS.F.00226]
 - 17 **Lévigne C**, Garret J, Boileau P, Alami G, Favard L, Walch G. Scapular notching in reverse shoulder arthroplasty: is it important to avoid it and how? *Clin Orthop Relat Res* 2011; **469**: 2512-2520 [PMID: 21116754 DOI: 10.1007/s11999-010-1695-8]
 - 18 **Nyffeler RW**, Werner CM, Gerber C. Biomechanical relevance of glenoid component positioning in the reverse Delta III total shoulder prosthesis. *J Shoulder Elbow Surg* 2005; **14**: 524-528 [PMID: 16194746 DOI: 10.1016/j.jse.2004.09.010]
 - 19 **Kempton LB**, Balasubramaniam M, Ankerson E, Wiater JM. A radiographic analysis of the effects of prosthesis design on scapular notching following reverse total shoulder arthroplasty. *J Shoulder Elbow Surg* 2011; **20**: 571-576 [PMID: 21167747 DOI: 10.1016/j.jse.2010.08.024]
 - 20 **Kowalsky MS**, Galatz LM, Shia DS, Steger-May K, Keener JD. The relationship between scapular notching and reverse shoulder arthroplasty prosthesis design. *J Shoulder Elbow Surg* 2012; **21**: 1430-1441 [PMID: 22079766 DOI: 10.1016/j.jse.2011.08.051]
 - 21 **Walch G**, Badet R, Boulahia A, Khoury A. Morphologic study of the glenoid in primary glenohumeral osteoarthritis. *J Arthroplasty* 1999; **14**: 756-760 [PMID: 10512449 DOI: 10.1016/S0883-5403(99)90232-2]
 - 22 **Koh KH**, Han KY, Yoon YC, Lee SW, Yoo JC. True anteroposterior (Grashey) view as a screening radiograph for further imaging study in rotator cuff tear. *J Shoulder Elbow Surg* 2013; **22**: 901-907 [PMID: 23312822 DOI: 10.1016/j.jse.2012.09.015]
 - 23 **Lévigne C**, Boileau P, Favard L, Garaud P, Molé D, Sirveaux F, Walch G. Scapular notching in reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2008; **17**: 925-935 [PMID: 18558499 DOI: 10.1016/j.jse.2008.02.010]
 - 24 **Kempton LB**, Balasubramaniam M, Ankerson E, Wiater JM. A radiographic analysis of the effects of glenosphere position on scapular notching following reverse total shoulder arthroplasty. *J Shoulder Elbow Surg* 2011; **20**: 968-974 [PMID: 21398149 DOI: 10.1016/j.jse.2010.11.026]
 - 25 **Weisberg S**. Applied Linear Regression. 2nd ed. New York: John Wiley & Sons, 1985
 - 26 **Frankle M**, Siegal S, Pupello D, Saleem A, Mighell M, Vasey M. The Reverse Shoulder Prosthesis for glenohumeral arthritis associated with severe rotator cuff deficiency. A minimum two-year follow-up study of sixty patients. *J Bone Joint Surg Am* 2005; **87**: 1697-1705 [PMID: 16085607 DOI: 10.2106/JBJS.D.02813]
 - 27 **Frankle M**, Levy JC, Pupello D, Siegal S, Saleem A, Mighell M, Vasey M. The reverse shoulder prosthesis for glenohumeral arthritis associated with severe rotator cuff deficiency. a minimum two-year follow-up study of sixty patients surgical technique. *J Bone Joint Surg Am* 2006; **88** Suppl 1 Pt 2: 178-190 [PMID: 16951091]
 - 28 **Clark JC**, Ritchie J, Song FS, Kissenberth MJ, Tolan SJ, Hart ND, Hawkins RJ. Complication rates, dislocation, pain, and postoperative range of motion after reverse shoulder arthroplasty in patients with and without repair of the subscapularis. *J Shoulder Elbow Surg* 2012; **21**: 36-41 [PMID: 21803609 DOI: 10.1016/j.jse.2011.04.009]
 - 29 **Mulieri P**, Dunning P, Klein S, Pupello D, Frankle M. Reverse shoulder arthroplasty for the treatment of irreparable rotator cuff tear without glenohumeral arthritis. *J Bone Joint Surg Am* 2010; **92**: 2544-2556 [PMID: 21048173 DOI: 10.2106/jbjs.i.00912]
 - 30 **Gutiérrez S**, Levy JC, Frankle MA, Cuff D, Keller TS, Pupello DR, Lee WE. Evaluation of abduction range of motion and avoidance of inferior scapular impingement in a reverse shoulder model. *J Shoulder Elbow Surg* 2008; **17**: 608-615 [PMID: 18325795 DOI: 10.1016/j.jse.2007.11.010]
 - 31 **Gutiérrez S**, Greiwe RM, Frankle MA, Siegal S, Lee WE. Bio-mechanical comparison of component position and hardware failure in the reverse shoulder prosthesis. *J Shoulder Elbow Surg* 2007; **16**: S9-S12 [PMID: 16990024 DOI: 10.1016/j.jse.2005.11.008]
 - 32 **Berhouet J**, Garaud P, Favard L. Evaluation of the role of glenosphere design and humeral component retroversion in avoiding scapular notching during reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2014; **23**: 151-158 [PMID: 23850310 DOI: 10.1016/j.jse.2013.05.009]
 - 33 **Wierks C**, Skolasky RL, Ji JH, McFarland EG. Reverse total shoulder replacement: intraoperative and early postoperative complications. *Clin Orthop Relat Res* 2009; **467**: 225-234 [PMID: 18685908 DOI: 10.1007/s11999-008-0406-1]
 - 34 **Kempton LB**, Ankerson E, Wiater JM. A complication-based learning curve from 200 reverse shoulder arthroplasties. *Clin Orthop Relat Res* 2011; **469**: 2496-2504 [PMID: 21328021 DOI: 10.1007/s11999-011-1811-4]

P- Reviewer: Metzger P, Sarda P **S- Editor:** Kong JX **L- Editor:** A
E- Editor: Lu YJ



Retrospective Cohort Study

Return to physical activity after gastrocnemius recession

Camelia Tang Qian Ying, Sean Lai Wei Hong, Bing Howe Lee, Gowreeson Thevendran

Camelia Tang Qian Ying, Sean Lai Wei Hong, Bing Howe Lee, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore

Gowreeson Thevendran, Department of Orthopaedic Surgery, Tan Tock Seng Hospital, Singapore 308433, Singapore

Author contributions: Tang Qian Ying C, Lai Wei Hong S, Lee BH and Thevendran G jointly designed and performed the research, analysed the data and wrote the paper.

Institutional review board statement: The study was reviewed and approved for publication by the institutional reviewer.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: All authors have no conflict of interest related to the manuscript.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Camelia Tang Qian Ying, Yong Loo Lin School of Medicine, National University of Singapore, NUHS Tower Block, Level 11, Singapore 117597, Singapore. camelia.cam.93@gmail.com
Telephone: +65-93215779

Received: July 18, 2016

Peer-review started: July 21, 2016

First decision: August 5, 2016

Revised: August 18, 2016

Accepted: September 7, 2016

Article in press: September 8, 2016

Published online: November 18, 2016

Abstract

AIM

To prospectively investigate the time taken and patients' ability to resume preoperative level of physical activity after gastrocnemius recession.

METHODS

Endoscopic gastrocnemius recession (EGR) was performed on 48 feet in 46 consecutive sportspersons, with a minimum follow-up of 24 mo. The Halasi Ankle Activity Score was used to quantify the level of physical activity. Time taken to return to work and physical activity was recorded. Functional outcomes were evaluated using the short form 36 (SF-36), American Orthopedic Foot and Ankle Society (AOFAS) Hindfoot score and modified Olerud and Molander (O and M) scores respectively. Patient's satisfaction and pain experienced were assessed using a modified Likert scale and visual analogue scales. P -value < 0.05 was considered statistically significant.

RESULTS

Ninety-one percent ($n = 42$) of all patients returned to their preoperative level of physical activity after EGR. The mean time for return to physical activity was 7.5 (2-24) mo. Ninety-eight percent ($n = 45$) of all patients were able to return to their preoperative employment status, with a mean time of 3.6 (1-12) mo. Ninety-six percent ($n = 23$) of all patients with an activity score > 2 were able to resume their preoperative level of physical activity in mean time of 8.8 mo, as compared to 86% ($n = 19$) of patients whose activity score was ≤ 2 , with mean time of 6.1 mo. Significant improvements were noted in SF-36, AOFAS hindfoot and modified O and M scores. Ninety percent of all patients rated good or very good outcomes on the Likert scale.

CONCLUSION

The majority of patients were able to return to their pre-operative level of sporting activity after EGR.

Key words: Endoscopic gastrocnemius release; Time return to work; Return to physical activity; Post-operative outcomes; Foot and ankle

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Whilst the biomechanical advantage of surgical off-loading from gastrocnemius recession is well proven, the potential for weak push-off strength post-operatively continues to be debated. We are not aware of any published literature investigating the impact of the gastrocnemius recession procedure on the ability to return to physical activity. This study aims to investigate the hypothesis that the majority of patients will be unable to return to their pre-operative level of physical activity after a gastrocnemius recession procedure.

Tang Qian Ying C, Lai Wei Hong S, Lee BH, Thevendran G. Return to physical activity after gastrocnemius recession. *World J Orthop* 2016; 7(11): 746-751 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/746.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.746>

INTRODUCTION

Gastrocnemius recession has evolved into a well-established surgical procedure that is increasingly performed in orthopaedic foot and ankle surgery. It is indicated primarily in individuals who experience symptoms from biomechanical overload caused by an equinus ankle resulting from a tight superficial posterior compartment musculature that restricts ankle dorsiflexion^[1]. Gastrocnemius contracture may result in an ankle equinus deformity which in turn alters the foot biomechanics and increases forefoot pressures^[2]. Gastrocnemius contracture has been implicated as the cause of a variety of foot and ankle pathologies including metatarsalgia^[3], diabetic foot ulcer^[4], pes planus deformity^[5], hallux valgus^[6] and plantar fasciitis^[7]. It is postulated this may be secondary to excessive forefoot loading and heel hypervalgus^[8]. The diagnosis of gastrocnemius tightness is primarily clinical using the Silfverskiöld test^[8]. The test is positive when an ankle dorsiflexion of less than or equal to 10° on knee extension is increased to more than 10° on knee flexion whilst the hindfoot is held in neutral^[9].

With the advent of minimally invasive surgical techniques and instruments to support it, an endoscopic approach to gastrocnemius recession has been proposed as an alternative to open gastrocnemius recession^[10]. The efficacy and safety profile of endoscopic gastrocnemius recession (EGR) has been investigated in a number of case series with the procedure being associated with a

shorter postoperative recovery, fewer wound-related complications and greater patient satisfaction^[10,11].

Complications of gastrocnemius recession has been well documented in the literature^[12]. Of these, the potential for significant plantarflexion weakness attributed to lengthening of the gastroc-soleus muscle unit^[13] has generated much concern amongst orthopaedic surgeons and sports medicine practitioners alike. Whilst the biomechanical advantage of surgical off-loading from gastrocnemius recession is well proven, the potential for weak push-off strength when performed in a sportsperson continues to remain a concern. We are not aware of any published literature investigating the impact of the gastrocnemius recession procedure on the ability to return to preoperative level of physical activity.

The primary aim of this study was to prospectively evaluate a consecutive series of patients undergoing gastrocnemius recession with regards to the time taken and their ability to return to preoperative level of physical activity. The secondary aim of the study was to evaluate the functional outcome and complication profile of the gastrocnemius recession procedure when performed endoscopically in a consecutive series of patients.

MATERIALS AND METHODS

Subjects

With Institutional Review Board approval, 48 feet (25 left and 23 right) in 46 consecutive patients (34 female and 12 male; mean age 49.7 ± 18.6 years; range 21 to 83 years) who underwent EGR through a single lateral portal using the Smart Release Endoscopic Carpal Tunnel Release System were included in the study (Table 1). All patients who were recruited for the procedure had an isolated gastrocnemius contracture which was confirmed clinically with the Silfverskiöld test. Patients with ankle joint pathology resulting in an equinus or spastic contractures secondary to neurological injury were excluded.

The same operative technique was applied to all patients and all procedures were performed by 2 senior foot and ankle fellowship trained orthopaedic surgeon at a single institution within a 3-year period. In all patients, the aponeurosis for both the medial and lateral heads of the gastrocnemius was released at the distal muscle-tendon junction.

Follow-up

The mean follow-up period was 32 ± 7.7 mo, with minimum duration of 24 mo (range 24 to 60 mo). The primary outcome measure recorded was the time taken from the operative day to a point in the future when the patient was able to participate in their preferred physical activity or sport at a level that was similar to their preoperative level of activity. In order to evaluate and stratify the level of physical activity pursued by the individual patient, the ankle activity score developed and validated by Halasi and associates^[14] was used. This 10-point scoring system is based on the type and level of physical activity, with 0 points indicating the lowest

Table 1 Patient demographics

Demographic	Value
No. of patients	46
No. of feet/recessions	48
Age	Mean: 49.73 ± 18.59 yr Range: 21 to 83 yr
Gender	Female: 35 Male: 13
Side of operation	Left: 25 (52.1%) Right: 23 (47.9%)
Follow-up months	Mean 32 ± 7.66 mo Range 24-60 mo

activity level and 10 points indicating the highest activity level. Time taken before patients returned to the same level of physical activity based on the Halasi score was recorded. As a surrogate marker of return to activity, time taken to return to full time employment was also recorded.

Secondary outcome measures were evaluated using validated scoring systems. Functional evaluation was carried out preoperatively, at 1 year and 2 years postoperatively using the short form 36 (SF-36), American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot score and Modified Olerud and Molander (O and M) Score. The Likert scale and visual analogue pain scores (VAS) were used to evaluate patient satisfaction and pain scores respectively.

The preoperative scoring was done during the preoperative clinic consultations whilst the postoperative scores were tabulated during postoperative consultation visits.

Statistical analysis

IBM SPSS Statistics version 20 was used to perform statistical analysis of the collected data. The analysis aimed to identify any significant change between the preoperative and 2-year postoperative scores of SF-36, AOFAS Hindfoot score, Modified O and M and VAS Scores. Paired parametric Student *t*-test was performed on the data sets. Descriptive statistics were used for the demographic variables. Results were expressed as means ± SD. A *P*-value of < 0.05 was considered statistically significant.

RESULTS

Functional outcome

Forty-two out of the 46 patients (91%) were able to return to their preoperative level of physical activity after EGR at the time of final follow-up. The mean duration of time taken to return to preoperative level of physical activity was 7.5 mo (range 2 to 24 mo). Of the 4 patients who failed to return to preoperative level of physical activity, at the 2-year follow-up, the first patient had dropped from a Halasi score of 4 to 2, the second patient a Halasi score 2 to 1 and the last two patients also dropped from Halasi scores 2 to 1. These final 2 patients

Table 2 Demographics of patients who successfully returned to preoperative level of physical activity and preoperative employment status

Halasi ankle activity score	No. of patients	Mean time to return to physical activity (mo)	Mean time to return to work (mo)
0	0	-	-
1	0	-	-
2	22	6.1	4.1
3	7	14.0	3.1
4	13	8.3	3.7
5	3	6.0	2.3
6	0	-	-
7	0	-	-
8	1	3.0	3.0
9	0	-	-
10	0	-	-
Total	46	7.5	3.6

were unable to return to physical activity due to other concomitant musculoskeletal problems (back and knee pathologies).

The mean duration of time taken to return to preoperative employment status for those who were engaged in employment (*n* = 37) was 3.6 mo (range 1 to 12 mo). Of the 37 patients analysed, 20 patients held sedentary desk-bound jobs. The time return to employment for this subset was 3.3 mo. In a further subset of 17 patients (35%) who held more physically demanding employment that necessitated them being on their feet for prolonged periods or performing manual tasks (salesperson, fitness instructors) the time return to employment was 3.9 mo. Overall, only 1 patient was unable to return to his original employment as a chef at the time of final follow-up due to persistent leg pains from prolonged standing.

When stratifying the level of physical activity using the Halasi ankle activity score, 22 patients (48%) claimed to participate only in low-intensity physical activity (defined as Halasi ankle activity score ≤ 2) whilst the remaining 24 patients (52%) participated in higher-intensity physical activity (defined as Halasi ankle activity score > 2) (Table 2).

Overall, 96% (*n* = 23) of those engaging in higher intensity activity (Halasi ankle activity score > 2) were able to return to their preoperative level of physical activity whilst only 86% (*n* = 19) of patients with Halasi ankle activity score ≤ 2 were able to do so. When comparing these 2 categories of patients, those with a Halasi ankle activity score of more than 2 reported a mean time return to activity of 8.8 mo (range 2 to 24 mo). In contrast, those with a Halasi ankle activity score of 2 or less reported a mean time return to activity of 6.1 mo (range 2 to 12 mo).

Secondary outcome measure

Preoperative, 1-year postoperative and 2-year postoperative SF-36, AOFAS, Modified O and M and VAS scores were obtained in all 46 patients. The preoperative and 1-year postoperative scores were compared and evaluated (Table 3).

Table 3 Summary of results (preoperative and 1-year postoperative)

Parameter	Preoperative Mean \pm SD	1 yr post-op Mean \pm SD	Improvements Mean \pm SD	P-value
SF-36				
Physical functioning	64.79 \pm 27.58	84.58 \pm 15.74	19.79 \pm 26.74	< 0.001
Role limitations due to physical health	45.83 \pm 41.68	84.38 \pm 23.98	38.54 \pm 42.83	< 0.001
Role limitation due to emotional problems	61.10 \pm 44.21	89.92 \pm 24.26	28.82 \pm 51.32	< 0.001
Energy/fatigue	60.42 \pm 18.24	65.63 \pm 15.80	5.21 \pm 14.95	0.02
Emotional well-being	74.00 \pm 16.46	74.04 \pm 17.40	0.04 \pm 18.46	0.988
Social functioning	74.79 \pm 21.23	96.25 \pm 7.20	21.46 \pm 22.51	< 0.001
Pain	60.78 \pm 21.38	91.30 \pm 12.48	30.52 \pm 24.17	< 0.001
General health	68.33 \pm 18.73	73.27 \pm 17.25	4.94 \pm 13.37	0.014
AOFAS Hindfoot Score	71.60 \pm 18.89	91.79 \pm 7.24	20.19 \pm 19.89	< 0.001
Modified Olerud and Molander score				
Pain	13.23 \pm 6.32	22.19 \pm 4.72	8.96 \pm 6.99	< 0.001
Stiffness	6.56 \pm 4.15	8.44 \pm 2.76	1.88 \pm 4.33	0.004
Swelling	7.60 \pm 3.57	8.54 \pm 2.91	0.94 \pm 4.46	0.152
Stair climbing	6.67 \pm 2.79	8.33 \pm 2.60	1.67 \pm 3.15	0.001
Running	1.56 \pm 2.34	2.29 \pm 2.52	0.73 \pm 1.78	0.007
Jumping	2.19 \pm 2.51	2.92 \pm 2.49	0.73 \pm 2.06	0.018
Squatting	4.38 \pm 1.67	4.48 \pm 1.54	0.10 \pm 1.93	0.71
Supports	7.92 \pm 3.69	8.85 \pm 2.78	0.94 \pm 3.67	0.083
Activities of daily life	0.00 \pm 0.00	17.08 \pm 4.59	17.08 \pm 4.59	< 0.001
Total	50.10 \pm 15.89	83.13 \pm 15.73	33.02 \pm 18.09	< 0.001
VAS	5.00 \pm 2.38	1.21 \pm 1.79	3.79 \pm 2.60	< 0.001

VAS: Visual analogue score; AOFAS: American Orthopedic Foot and Ankle Society.

When comparing functional outcomes at 1-year postoperative, there were significant improvements in all domains of the SF-36 questionnaire except for emotional well-being. There was significant improvement in AOFAS Hindfoot score of 20.19 ± 19.89 ($P < 0.001$), from a mean of 71.60 ± 18.89 preoperatively to 1-year postoperative mean of 91.79 ± 7.24 . There was also significant improvement in modified O and M score at the 1-year postoperative mark, with significant improvements in 7 out of the 9 domains of the O and M score.

Comparing 1-year postoperative and 2-year postoperative scores (Table 4), there were no statistically significant improvements in the domains of SF-36 questionnaire as well as the AOFAS Hindfoot scores. The modified O and M Score showed significant improvements in only the total score and in 2 out of 9 domains. This suggests that there are no significant ongoing improvements beyond the first year postoperative mark.

Analysis of the VAS score showed significant improvements at both the 1-year and 2-year postoperative marks, with a mean score improvement of 3.79 ± 2.60 ($P < 0.001$) and 4.31 ± 2.45 ($P < 0.001$) respectively. Beyond the first year, there was significant improvement of pain reduction between the first year and second year postoperatively, with improvements of 0.52 ± 1.17 ($P = 0.003$). Ninety percent of all cases reported good or very good outcomes on the Likert scale at the 2-year postoperative follow-up.

DISCUSSION

To ensure a more clinically relevant measurement of return to physical activity, the level of physical activity

was first stratified in this study. The Halasi Ankle Activity score is a validated tool designed specifically for the ankle and enabled a more accurate stratification of the intensity of physical activity pursued by individual patients. Time taken before being able to return to the same intensity of ankle activity postoperatively was used as an objective measure of time taken to return to physical function and a surrogate marker of any permanent functional deficit that may have resulted from the procedure. Similarly, time taken to return to preoperative level of employment was measured to reflect on the economic burden this procedure may have on an individual patient.

In this study, patients with a preoperative Halasi ankle activity score of more than 2 required a longer time to resume their physical activity to the same intensity level when compared to those with Halasi ankle activity score of 2 or less. However, 96% of all patients in the higher level activity group successfully regained their preoperative intensity of physical activity in contrast to only 86% in the second group. This result suggests gastrocnemius recession is unlikely to result in any permanent functional deficit that may compromise return to a higher level of physical activity or sport. We postulate the difference in time taken to return to physical activity in the two groups is likely attributable to higher levels of physical activities necessitating a more prolonged rehabilitation period.

For the cohort of employed patients ($n = 37$), the mean time to return to full time preoperative employment status was 3.6 mo (range 1 to 12 mo). This information is important to highlight to patients, especially those concerned about the ability to resume their occupation, during the peri-operative counselling period when

Table 4 Summary of results (1-year postoperative and 2-year postoperative)

Parameter	1 yr postoperative Mean \pm SD	2 yr postoperative Mean \pm SD	Improvements Mean \pm SD	P-value
SF-36				
Physical functioning	84.58 \pm 15.74	87.08 \pm 14.40	19.79 \pm 26.74	0.144
Role limitations due to physical health	84.38 \pm 23.98	88.13 \pm 23.58	38.54 \pm 42.83	0.169
Role limitation due to emotional problems	89.92 \pm 24.26	90.26 \pm 18.16	28.82 \pm 51.32	0.880
Energy/fatigue	65.63 \pm 15.80	63.85 \pm 15.51	5.21 \pm 14.95	0.290
Emotional well-being	74.04 \pm 17.40	76.02 \pm 13.50	0.04 \pm 18.46	0.274
Social functioning	96.25 \pm 7.20	95.63 \pm 9.07	21.46 \pm 22.51	0.566
Pain	91.30 \pm 12.48	92.43 \pm 13.72	30.52 \pm 24.17	0.401
General health	73.27 \pm 17.25	74.44 \pm 18.23	4.94 \pm 13.37	0.469
AOFAS Hindfoot Score	91.79 \pm 7.24	93.48 \pm 7.81	1.69 \pm 5.83	0.051
Modified Olerud and Molander score				
Pain	22.19 \pm 4.72	22.71 \pm 4.37	0.52 \pm 2.36	0.133
Stiffness	8.44 \pm 2.76	8.85 \pm 2.58	0.42 \pm 2.27	0.209
Swelling	8.54 \pm 2.91	8.85 \pm 2.36	0.31 \pm 1.90	0.261
Stair climbing	8.33 \pm 2.60	8.75 \pm 2.19	0.42 \pm 2.02	0.159
Running	2.29 \pm 2.52	3.23 \pm 2.42	0.94 \pm 1.97	0.002 ^a
Jumping	2.92 \pm 2.49	3.23 \pm 2.42	0.31 \pm 1.90	0.261
Squatting	4.48 \pm 1.54	4.48 \pm 1.54	0.00 \pm 1.03	1
Supports	8.85 \pm 2.78	9.58 \pm 1.74	0.73 \pm 2.06	0.018 ^a
Activities of daily life	17.08 \pm 4.59	17.71 \pm 3.85	0.63 \pm 3.66	0.243
Total	83.13 \pm 15.73	87.08 \pm 15.74	3.96 \pm 10.05	0.009 ^a
VAS	1.21 \pm 1.79	0.69 \pm 1.72	0.52 \pm 1.17	0.003 ^a

^aDenotes significant *P* values. VAS: Visual analogue score; AOFAS: American Orthopedic Foot and Ankle Society.

discussing the anticipated time away from work. Only 1 patient was unable to return to employment at the 2-year follow-up due to leg pains from prolonged standing as part of his job as a chef. The same patient was unable to return to his preoperative level of physical activity and this was attributed to the presence of other concomitant lower back pain and not the gastrocnemius recession procedure alone.

The functional outcomes related to the single portal EGR was also evaluated in this study. The SF-36 scores showed statistically significant improvements in 6 out of 8 components while the modified O and M score revealed statistically significant improvements in 7 out of 9 domains. The AOFAS Hindfoot scores revealed significant improvements between preoperative and 2-year postoperative scores as well. Significant pain relief and high satisfaction rates were reflected by improvements in the VAS score and either good or very good outcomes on the Likert scale. These results are consistent with those from other studies in the current literature^[12,13].

Limitation and strength of the study

There are several limitations to this study. Firstly, this is a single centre series of 46 patients. A larger pool of patients would increase the power of analysis for return to physical activity. Secondly, there were no comparisons made with alternative techniques for gastrocnemius recession and it is conceivable that a different surgical technique may influence time return to physical activity, though there is a paucity of evidence to substantiate this. Finally, patients were not matched for other concurrent musculoskeletal pathology and it is feasible that time return to physical activity may be influenced by other comorbidities.

The primary strength of this study is its novelty in addressing the clinically relevant question of what is the likelihood of return to physical functional activity after a gastrocnemius recession procedure. The minimum follow-up of 24 mo, use of validated functional and activity scoring plus consistency in the surgical technique substantiates the role of this procedure in our therapeutic armamentarium.

The result of this study shows that a vast majority (91%) of patients post gastrocnemius release regained their preoperative level of physical activity after a mean of 7.5 mo. As expected, there is a trend towards a longer recovery period for those who participate in higher level of physical activity. There are significant functional improvements and pain relief following this procedure as assessed at the 2-year postoperative mark.

COMMENTS

Background

Endoscopic gastrocnemius release (EGR) has evolved into a popular procedure that reliably treats ankle equinus from a tight gastrocnemius contracture. There is however considerable anxiety amongst surgeons who perform this procedure that it may result in permanent ankle plantarflexion weakness, thereby preventing return to pre-operation level of physical activity.

Research frontiers

The efficacy and safety profile of EGR has been investigated in a number of case series with the procedure being associated with a shorter postoperative recovery, fewer wound-related complications and greater patient satisfaction.

Innovations and breakthroughs

The potential for significant plantarflexion weakness attributed to lengthening of the gastroc-soleus muscle unit has generated much concern amongst orthopaedic surgeons and sports medicine practitioners alike. This study aims to evaluate the novel clinical question of time taken to return to pre-operative

level of physical activity after EGR.

Applications

The majority of patients are able to return to their pre-operative level of sporting activity after EGR. Ninety-one percent ($n = 42$) of all patients returned to their preoperative level of physical activity after EGR. The mean time for return to physical activity was 7.5 (2-24) mo. Ninety-eight percent ($n = 45$) of all patients were able to return to their preoperative employment status, with a mean time of 3.6 (1-12) mo. Ninety-six percent ($n = 23$) of all patients with an activity score > 2 were able to resume their preoperative level of physical activity in mean time of 8.8 mo, as compared to 86% ($n = 19$) of patients whose activity score was ≤ 2 , with mean time of 6.1 mo.

Terminology

About endoscopic gastrocnemius recession: A variety of muscle-tendon unit release procedures along the calf such as Silfverskoid, Baumann, Vulpius, Baker and Strayer procedure, have been described over the past century. These involve at least a partial or complete release of the gastrocnemius muscle to diminish its role as the primary plantarflexor of the ankle. Of the many recession techniques that have been described, the one described by Strayer has gained most popularity. Traditionally performed as an open procedure, the Strayer procedure involves making an incision on the ventral surface of the calf and releasing only the gastrocnemius aponeurosis just distal to its muscle belly. With the advent of minimally invasive surgical techniques and instruments to support it, an endoscopic approach to gastrocnemius recession has been popularised as an alternative to open gastrocnemius recession.

Peer-review

This is an interesting research article on the return to physical activity after gastrocnemius recession procedure. In general, the methodology is appropriate, the results are clinically significant, and the implication for clinical practice is quite useful.

REFERENCES

- 1 **Cychosz CC**, Phisitkul P, Belatti DA, Glazebrook MA, DiGiovanni CW. Gastrocnemius recession for foot and ankle conditions in adults: Evidence-based recommendations. *Foot Ankle Surg* 2015; **21**: 77-85 [PMID: 25937405 DOI: 10.1016/j.fas.2015.02.001]
- 2 **Macklin K**, Healy A, Chockalingam N. The effect of calf muscle stretching exercises on ankle joint dorsiflexion and dynamic foot pressures, force and related temporal parameters. *Foot (Edinb)* 2012; **22**: 10-17 [PMID: 21944945 DOI: 10.1016/j.foot.2011.09.001]
- 3 **Maskill JD**, Bohay DR, Anderson JG. Gastrocnemius recession to treat isolated foot pain. *Foot Ankle Int* 2010; **31**: 19-23 [PMID: 20067718 DOI: 10.3113/FAI.2010.0019]
- 4 **Hastings MK**, Mueller MJ, Sinacore DR, Salsich GB, Engsborg JR, Johnson JE. Effects of a tendo-Achilles lengthening procedure on muscle function and gait characteristics in a patient with diabetes mellitus. *J Orthop Sports Phys Ther* 2000; **30**: 85-90 [PMID: 10693086 DOI: 10.2519/jospt.2000.30.2.85]
- 5 **Meszaros A**, Caudell G. The surgical management of equinus in the adult acquired flatfoot. *Clin Podiatr Med Surg* 2007; **24**: 667-685, viii [PMID: 17908636 DOI: 10.1016/j.cpm.2007.07.007]
- 6 **Aronow MS**, Diaz-Doran V, Sullivan RJ, Adams DJ. The effect of triceps surae contracture force on plantar foot pressure distribution. *Foot Ankle Int* 2006; **27**: 43-52 [PMID: 16442028 DOI: 10.1177/107110070602700108]
- 7 **Downey MS**, Banks AS. Gastrocnemius recession in the treatment of nonspastic ankle equinus. A retrospective study. *J Am Podiatr Med Assoc* 1989; **79**: 159-174 [PMID: 2732918 DOI: 10.7547/87507315-79-4-159]
- 8 **Barouk P**, Barouk LS. Clinical diagnosis of gastrocnemius tightness. *Foot Ankle Clin* 2014; **19**: 659-667 [PMID: 25456715 DOI: 10.1016/j.fcl.2014.08.004]
- 9 **Singh D**. Nils Silfverskiöld (1888-1957) and gastrocnemius contracture. *Foot Ankle Surg* 2013; **19**: 135-138 [PMID: 23548458 DOI: 10.1016/j.fas.2012.12.002]
- 10 **Trevino S**, Gibbs M, Panchbhavi V. Evaluation of results of endoscopic gastrocnemius recession. *Foot Ankle Int* 2005; **26**: 359-364 [PMID: 15913518 DOI: 10.1177/107110070502600503]
- 11 **Phisitkul P**, Rungprai C, Femino JE, Arunakul M, Amendola A. Endoscopic Gastrocnemius Recession for the Treatment of Isolated Gastrocnemius Contracture: A Prospective Study on 320 Consecutive Patients. *Foot Ankle Int* 2014; **35**: 747-756 [PMID: 24850159 DOI: 10.1177/1071100714534215]
- 12 **DiDomenico LA**, Adams HB, Garchar D. Endoscopic gastrocnemius recession for the treatment of gastrocnemius equinus. *J Am Podiatr Med Assoc* 2005; **95**: 410-413 [PMID: 16037561 DOI: 10.7547/0950410]
- 13 **Delp SL**, Statler K, Carroll NC. Preserving plantar flexion strength after surgical treatment for contracture of the triceps surae: a computer simulation study. *J Orthop Res* 1995; **13**: 96-104 [PMID: 7853110 DOI: 10.1002/jor.1100130115]
- 14 **Halasi T**, Kynsburg A, Tállay A, Berkes I. Development of a new activity score for the evaluation of ankle instability. *Am J Sports Med* 2004; **32**: 899-908 [PMID: 15150035 DOI: 10.1177/0363546503262181]

P- Reviewer: Chen GS, Godoy-Santos AL, Spiegel DA
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Lu YJ



Retrospective Study

Improvements after mod Quad and triangle tilt revision surgical procedures in obstetric brachial plexus palsy

Rahul K Nath, Chandra Somasundaram

Rahul K Nath, Chandra Somasundaram, Texas Nerve and Paralysis Institute, Houston, TX 77030, United States

Author contributions: Nath RK conceived of the study, performed all the surgeries and revised the manuscript; Somasundaram C participated in the design of the study, performed the statistical analysis and drafted the manuscript; both authors read and approved the final manuscript.

Institutional review board statement: This was a retrospective study of patient charts, which exempted it from the need for IRB approval in the United States. Patients were treated ethically in compliance with the Helsinki declaration. Documented informed consent was obtained for all patients.

Informed consent statement: Written informed consent was obtained from all patients for publication and accompanying images. A copy of the written consent is available for review on request.

Conflict-of-interest statement: The authors report that there are no conflicts of interest.

Data sharing statement: No.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Rahul K Nath, Texas Nerve and Paralysis Institute, 6400. Fannin St., Houston, TX 77030, United States. drnath@drnathmedical.com
 Telephone: +1-713-5909900
 Fax: +1-713-5909921

Received: March 23, 2016

Peer-review started: March 24, 2016
 First decision: July 5, 2016
 Revised: August 6, 2016
 Accepted: September 7, 2016
 Article in press: September 8, 2016
 Published online: November 18, 2016

Abstract

AIM

To compare outcomes of our revision surgical operations in obstetric brachial plexus palsy (OBPP) patients to results of conventional operative procedures at other institutions.

METHODS

We analyzed our OBPP data and identified 10 female and 10 male children aged 2.0 to 11.8 years (average age 6.5 years), who had prior conventional surgical therapies at other clinics. Of the 20 patients, 18 undergone triangle tilt, 2 had only mod Quad. Among 18 patients, 8 had only triangle tilt and 10 had also mod Quad as revision surgeries with us. We analyzed the anatomical improvements and functional modified Mallet statistically before and after a year post-revision operations.

RESULTS

Pre-revision surgery average modified Mallet score was 12.0 ± 1.5 . This functional score was greatly improved to 18 ± 2.3 ($P < 0.0001$) at least one-year after revision surgical procedures. Radiological scores (PHHA and glenoid version) were also improved significantly to 31.9 ± 13.6 ($P < 0.001$), -16.3 ± 11 ($P < 0.0002$), at least one-year after triangle tilt procedure. Their mean pre-triangle tilt (yet after other surgeon's surgeries) PHHA, glenoid version and SHEAR were 14.6 ± 21.7 , -31.6 ± 19.3 and 16.1 ± 14.7 respectively.

CONCLUSION

We demonstrate here, mod Quad and triangle tilt as

successful revision surgical procedures in 20 OBPP patients, who had other surgical treatments at other clinics before presenting to us for further treatment.

Key words: Revision surgery; Obstetric brachial plexus palsy; Shoulder movements; Joint incongruity; Upper limb

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We compared functional and anatomical improvements from our revision surgical treatment experiences to outcomes of other surgical treatments at other institutions in 20 obstetric brachial plexus palsy (OBPP) children. Pre-revision surgery mean modified Mallet scores and shoulder anatomical measurements were improved statistically highly significantly at least one-year after revision surgeries. We demonstrate here, mod Quad and triangle tilt as successful revision surgical procedures in 20 OBPP patients, who had other surgical treatments at other clinics before presenting to us for further treatment.

Nath RK, Somasundaram C. Improvements after mod Quad and triangle tilt revision surgical procedures in obstetric brachial plexus palsy. *World J Orthop* 2016; 7(11): 752-757 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/752.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.752>

INTRODUCTION

Poor recovery of neurological function in obstetric brachial plexus palsy (OBPP) results in muscle weakness and imbalances around the shoulder^[1-3]. Progressive muscle imbalance causes bony deformities at the shoulder joint, affecting its movements and functions^[4,5]. Many traditional surgical interventions have been reported to improve the upper extremity functions in OBPP patients^[6-11].

Muscle release and tendon transfer procedures have been shown^[12-19] to reduce the muscle contractures and improve shoulder movements. Humeral rotational osteotomy corrects the arm at resting position, but does not address the glenohumeral and *Scapular Hypoplasia, Elevation and Rotation* (SHEAR) deformities. These surgical treatments do not address these two osseous deformities.

We have published extensively the effectiveness of triangle tilt surgery in correcting glenohumeral joint incongruity and thereby improving upper extremity functions in OBPP patients^[20-28]. Here, we show both functional and anatomical improvements significantly after triangle tilt and or mod Quad as revision surgeries in 20 OBPP patients, who had other surgical treatments at outside clinics before visiting our clinic for further treatment.

MATERIALS AND METHODS

We analyzed our OBPP data and identified 10 female and 10 male patients, aged 2.0 to 11.8 years (average age 6.5 years), who had operative procedures at other clinics.

Of the 20 OBPP patients in our present study group, 8 patients undergone only the bony procedure, triangle tilt and 10 had both triangle tilt and mod Quad (Tables 1 and 2). Therefore, these 18 patients (Table 2) have anatomical and radiological scores (PHHA, SHEAR and glenoid version), in addition to functional modified Mallet scale (Table 1). Two patients, number 19 and 20 in Table 1, underwent only mod Quad procedure, as they did not have shoulder subluxation. Therefore, these two patients did not need to undergo triangle tilt procedure, which addresses shoulder subluxation. Modified Mallet and radiological scores were measured, statistically analyzed to compare. All measurements were done at least one-year after surgical treatments.

The nerve involvement was C5-6 ($n = 5$), C5-7 ($n = 8$), and total ($n = 7$). Traditional operative procedures that these OBPP children had in the past at other clinics are nerve transfer/graft, neurolysis, brachial plexus exploration, botox, muscle/tendon transfer and release, humeral osteotomy and anterior capsule release. Outcomes of our revision procedures in OBPP patients were compared to the results of other traditional surgical treatments at other clinics. Further, these patients' radiological scores were measured from computed tomography and magnetic resonance images and statistically compared.

Patient examination

We examined physically all OBPP children and their video recordings pre- and post-operatively, scoring their modified Mallet parameters on a scale between one and five. One and five denote lack of movement and normal function respectively.

Anatomical measurements of shoulder

We measured PHHA, glenoid version^[29] and Scapular hypoplasia, elevation and rotation^[30] using computed tomography and magnetic resonance imaging pre- and post-TT operative procedure.

Operative technique

Triangle tilt^[20-28] and mod Quad procedures^[14,31,32] have been demonstrated successful outcomes in OBPP.

We used the student's *t* test and compared pre- and post-operative results in this group of OBPP. $P < 0.05$ was considered statistically significant.

RESULTS

Pre-revision surgery mean modified Mallet score was 12.0 ± 1.5 (Table 1 and Figure 1 upper panels). This functional score was greatly improved to 18 ± 2.3 ($P <$

Table 1 Comparing functional improvements of other surgeon’s surgeries to mod Quad and/or triangle tilt in obstetric brachial plexus palsy

Patients	Other surgeons’ surgery	Gender	Age (yr)	Nerve involved	TT/MQ	Total Mallet pre-revision surgery	Total Mallet post-revision surgery
1	Botox	F	2.5	C5-C7	TT	13	23
2	Partial MQ, subscap release lat dorsi rerouting	M	6.4	C5-C7	TT	11	16
3	Neurolysis/nerve graft	F	4.2	Total	TT and MQ	13	18
4	Humeral osteotomy	F	11.1	C5-C7	TT and MQ	11	15
5	Neuroma excision, nervegraft	M	11.8	Total	TT	11	14
6	Nerve graft, HO, botox	F	7.1	Total	TT	11	17
7	Coracoacromial release/coracoid resection	M	5.5	C5-C7	TT	14	21
8	Botox	M	11.3	C5-C7	TT and MQ	10	15
9	Sural nerve graft	F	5.0	Total	TT	10	17
10	Botox	M	3.5	C5-C6	TT and MQ	12	20
11	Botox	M	4.3	Total	TT and MQ	12	18
12	Neurolysis	F	2.0	C5-C6	TT and MQ	11	17
13	Capsule release	F	8.5	Total	TT and MQ	13	19
14	Tendon transfer, neurolysis	M	4.3	C5-C8	TT and MQ	14	20
15	Neurolysis and botox	F	5.0	C5-C6	TT	13	20
16	Muscle transfer	M	7.9	C5-C7	TT	14	21
17	BP exploration	M	2.0	C5-C6	TT and MQ	15	20
18	Steindler flexorplasty	F	10.0	C5-C7	TT and MQ	13	18
19	Humeral osteotomy	M	14.0	C5-C6	MQ	12	18
20	Tendon transfer	F	3.0	C5-C7	MQ	14	20
	Mean ± STD		6.5			12 ± 1.5	18 ± 2.3
	P value					< 0.0001	

MQ: Mod Quad; HO: Humeral osteotomy.

Table 2 Comparing anatomical improvements of triangle tilt to other surgeon surgeries in obstetric brachial plexus palsy

Patients	Other surgeons and previous surgeries	PreTT-PHHA	PostTT-PHHA	PreTT-Version	PostTT-Version	PreTT-SHEAR	PostTT-SHEAR
1	Subscap release and lat dorsi rerouting	8	33	-47	-14		
2	Neurolysis, MQ, HO	16	14	-41	-35	24	10
3	MQ	-12	19	-65	-33	40	39
4	Nerve graft, FO, BTL, MQ	32	37	-21	-10	3	1
5	Botox, MQ	33	45	-18	-15	15	3
6	Nerve graft	47	48	-10	-1	5	14
7	Neurolysis, nerve graft	-7	22	-62	-12	8	22
8	Neuroma excision, nerve graft	34	35	-20	-11	0	0
9	Nerve transfer	33	29	-16	-21	15	12
10	Coracoacromial release/resection	-12	17	-51	-35	30	15
11	Neurolysis, nerve graft	13	4	-20	-15	7	4
12	Wrist Caps, HO	39	50	0	0	9	0
13	Sural nerve graft	38	51	-10	-4	0	1
14	Botox, MQ	-8	44	-38	-22	11	2
15	Neurolysis, MQ	-14	35	-33	-10	25	30
16	Muscle release	0	19	-45	-27	32	8
17	Anterior capsule release	-11	34	-53	-22	48	41
18	Tendon transfer and neurolysis	33	39	-18	-7	1	1
Mean		14.6 ±	31.9 ±	-31.6 ±	-16.3 ±	16.1 ±	11.9 ±
STD		21.7	13.6	19.3	11.0	14.7	13.5
P value			0.001		0.0002		0.087

Normal values are PHHA 50, glenoid version and SHEAR 0. TT: Triangle Tilt; MQ: Mod Quad; HO: Humeral Osteotomy; FO: Forearm Osteotomy; BTL: Biceps Tendon Lengthening; PHHA: Percentage of the Humeral Head Anterior.

0.0001) at least one-year after our revision surgeries (Table 1, Figure 1 lower panels). Furthermore, their shoulder anatomical scores were improved significantly to 31.9 ± 13.6 (*P* < 0.001) and -16.3 ± 11 (*P* < 0.0002) at least one-year after triangle tilt operation (Table 2 and Figure 2, lower panels). This was in comparison to their radiological outcomes of other procedures before

having triangle tilt with us (mean PHHA, glenoid version and SHEAR were 14.6 ± 21.7, -31.6 ± 19.3 and 16.1 ± 14.7 respectively; Table 2 and Figure 2 upper panels).

DISCUSSION

Twenty OBPP children in our present study had one or



Figure 1 Modified Mallet functions performed by an obstetric brachial palsy child, who had surgeries at other clinics before presenting to us (upper panels) and the same child, at least one-year after having mod Quad and triangle tilt as revision surgeries at our clinic (lower panels).

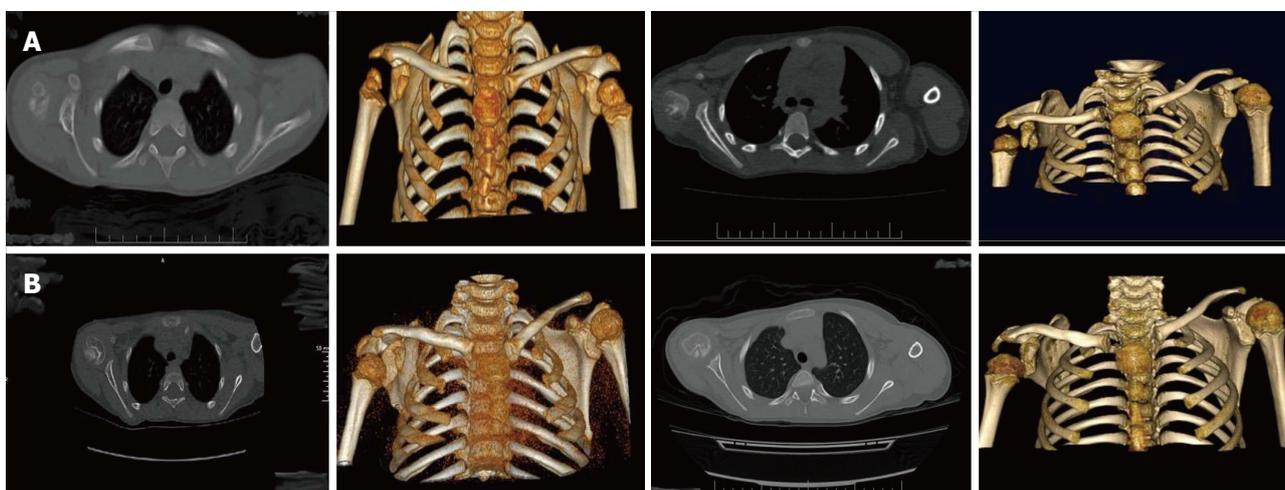


Figure 2 Comparison of computed tomography images of obstetric brachial palsy children, who had surgeries at other clinics before presenting to us (A) and the computed tomography images of the same children at least one-year after having triangle tilt as revision surgery at our clinic (B).

multiple operative procedures at other clinics before visiting our institute for further treatments (Table 1). One patient in our study group had Steindler flexoroplasty, which improves active flexion of the elbow. These conventional treatments fail to address the SHEAR deformity^[30] associated with majority of OBPP patients. Therefore, these OBPP patients in our study had persistent shoulder contractures and joint incongruity. Hence, they also had poor upper extremity functions. (Tables 1 and 2; upper panels in Figures 1 and 2).

Mod Quad procedure addresses poor shoulder ab-

duction in permanent OBPP. However, this procedure is ineffective to correct the glenohumeral joint and SHEAR deformities. Eighteen OBPP children, who had shoulder joint incongruity and SHEAR undergone TT bony operation with us. We demonstrated that this procedure effectively addressed the bony deformities of the affected upper extremity and improved its anatomy and functions^[20-28]. After undergone these two revision surgical procedures with us, these twenty patients had better results both functionally and anatomically. This is highly significant in comparison to the outcomes of

other surgical treatments at other clinics.

There was statistically significant improvement anatomically, after having triangle tilt compared to the radiological outcomes of other operative procedures.

In conclusion, we demonstrate here that mod Quad and triangle tilt as successful revision surgical procedures in 20 OBPP patients, who had conventional surgical therapies at other clinics before presenting to us for further treatment.

COMMENTS

Background

Many traditional surgical interventions such as posterior glenohumeral capsulorrhaphy, biceps tendon lengthening, humeral osteotomy, anterior capsule release, nerve transfer/graft, botox, muscle and or tendon transfer and release have been reported to improve upper limb functions in obstetric brachial plexus palsy (OBPP) patients.

Research frontiers

The authors compared functional and anatomical improvements from the revision surgical treatment experiences to results of other traditional surgeries at other clinics in 20 children with OBPP.

Innovations and breakthroughs

Pre-revision surgery mean mod Mallet scores and radiological scores such as posterior subluxation and glenoid version were improved statistically highly significantly at least one-year after mod Quad and or triangle tilt revision surgeries.

Applications

The authors demonstrate here, the triangle tilt and mod Quad as successful revision surgeries in OBPP patients, who had other surgical treatments at other clinics.

Terminology

SHEAR: Scapular Hypoplasia, Elevation and Rotation; Triangle tilt surgery: This surgical procedure includes osteotomies of the clavicle, neck of the acromion and scapula in order to release the distal acromioclavicular triangle and allow it to reorient itself in a more neutral position into the glenoid.

Peer-review

This is an informative paper, generally well-written and of interest to readers.

REFERENCES

- 1 **Birch R.** Late sequelae at the shoulder in obstetrical palsy in children. Surgical techniques in orthopaedics and traumatology: Shoulder. Volume 3. In: Randelli M, Karlsson J, editors. *Surgical Techniques in Orthopaedics and Traumatology*. Paris: Elsevier, 2001: 55-200-E-210
- 2 **Kon DS, Darakjian AB, Pearl ML, Kosco AE.** Glenohumeral deformity in children with internal rotation contractures secondary to brachial plexus birth palsy: intraoperative arthrographic classification. *Radiology* 2004; **231**: 791-795 [PMID: 15163819 DOI: 10.1148/radiol.2313021057]
- 3 **van der Sluijs JA, van Ouwkerk WJ, de Gast A, Wuisman PI, Nollet F, Manoliu RA.** Deformities of the shoulder in infants younger than 12 months with an obstetric lesion of the brachial plexus. *J Bone Joint Surg Br* 2001; **83**: 551-555 [PMID: 11380130 DOI: 10.1302/0301-620X.83B4.11205]
- 4 **Waters PM.** Obstetric Brachial Plexus Injuries: Evaluation and Management. *J Am Acad Orthop Surg* 1997; **5**: 205-214 [PMID: 10797223 DOI: 10.5435/00124635-199707000-00004]
- 5 **Birch R, Bonney G, Wynn Parry CB.** Birth lesions of the brachial plexus. In *Surgical disorders of the peripheral nerves*. In: Birch R, Bonney G, Wynn Parry CB, editors. New York, NY: Churchill Livingstone, 1998: 209-233
- 6 **Shenaq SM, Kim JY, Armenta AH, Nath RK, Cheng E, Jedrysiak A.** The Surgical Treatment of Obstetric Brachial Plexus Palsy. *Plast Reconstr Surg* 2004; **113**: 54E-67E [PMID: 15083009 DOI: 10.1097/01.PRS.0000110215.61220.72]
- 7 **Nath RK, Somasundaram C, Mahmooduddin F.** Comparing functional outcome of triangle tilt surgery performed before versus after two years of age. *Open Orthop J* 2011; **5**: 59-62 [PMID: 21566737 DOI: 10.2174/1874325001105010059]
- 8 **Hoffer MM, Phipps GJ.** Closed reduction and tendon transfer for treatment of dislocation of the glenohumeral joint secondary to brachial plexus birth palsy. *J Bone Joint Surg Am* 1998; **80**: 997-1001 [PMID: 9698004]
- 9 **Pearl ML, Edgerton BW, Kon DS, Darakjian AB, Kosco AE, Kazimiroff PB, Burchette RJ.** Comparison of arthroscopic findings with magnetic resonance imaging and arthrography in children with glenohumeral deformities secondary to brachial plexus birth palsy. *J Bone Joint Surg Am* 2003; **85-A**: 890-898 [PMID: 12728041]
- 10 **Pedowitz DI, Gibson B, Williams GR, Kozin SH.** Arthroscopic treatment of posterior glenohumeral joint subluxation resulting from brachial plexus birth palsy. *J Shoulder Elbow Surg* 2007; **16**: 6-13 [PMID: 17055299 DOI: 10.1016/j.jse.2006.04.008]
- 11 **Kambhampati SB, Birch R, Cobiella C, Chen L.** Posterior subluxation and dislocation of the shoulder in obstetric brachial plexus palsy. *J Bone Joint Surg Br* 2006; **88**: 213-219 [PMID: 16434527 DOI: 10.1302/0301-620X.88B2.17185]
- 12 **Al-Qattan MM.** Latissimus dorsi transfer for external rotation weakness of the shoulder in obstetric brachial plexus palsy. *J Hand Surg Br* 2003; **28**: 487-490 [PMID: 12954263 DOI: 10.1016/S0266-7681(02)00393-5]
- 13 **El-Gammal TA, Saleh WR, El-Sayed A, Kotb MM, Imam HM, Fathi NA.** Tendon transfer around the shoulder in obstetric brachial plexus paralysis: clinical and computed tomographic study. *J Pediatr Orthop* 2006; **26**: 641-646 [PMID: 16932105 DOI: 10.1097/01.bpo.0000229975.86188.c4]
- 14 **Nath RK, Paizi M.** Improvement in abduction of the shoulder after reconstructive soft-tissue procedures in obstetric brachial plexus palsy. *J Bone Joint Surg Br* 2007; **89**: 620-626 [PMID: 17540747 DOI: 10.1302/0301-620X.89B5.18403]
- 15 **Pagnotta A, Haerle M, Gilbert A.** Long-term results on abduction and external rotation of the shoulder after latissimus dorsi transfer for sequelae of obstetric palsy. *Clin Orthop Relat Res* 2004; 199-205 [PMID: 15346074 DOI: 10.1097/01.blo.0000138957.11939.70]
- 16 **Safoury Y.** Muscle transfer for shoulder reconstruction in obstetrical brachial plexus lesions. *Handchir Mikrochir Plast Chir* 2005; **37**: 332-336 [PMID: 16287018 DOI: 10.1055/s-2005-872818]
- 17 **van der Sluijs JA, van Ouwkerk WJ, de Gast A, Nollet F, Winters H, Wuisman PI.** Treatment of internal rotation contracture of the shoulder in obstetric brachial plexus lesions by subscapular tendon lengthening and open reduction: early results and complications. *J Pediatr Orthop B* 2004; **13**: 218-224 [PMID: 15083126 DOI: 10.1097/01202412-200405000-00015]
- 18 **Waters PM, Bae DS.** The effect of derotational humeral osteotomy on global shoulder function in brachial plexus birth palsy. *J Bone Joint Surg Am* 2006; **88**: 1035-1042 [PMID: 16651578 DOI: 10.2106/JBJS.E.00680]
- 19 **Waters PM, Bae DS.** Effect of tendon transfers and extra-articular soft-tissue balancing on glenohumeral development in brachial plexus birth palsy. *J Bone Joint Surg Am* 2005; **87**: 320-325 [PMID: 15687154 DOI: 10.2106/JBJS.C.01614]
- 20 **Nath RK, Amrani A, Melcher SE, Eichhorn MG.** Triangle tilt surgery in an older pediatric patient with obstetric brachial plexus injury. *Eplasty* 2009; **9**: e26 [PMID: 19641599]
- 21 **Nath RK, Amrani A, Melcher SE, Wentz MJ, Paizi M.** Surgical normalization of the shoulder joint in obstetric brachial plexus injury. *Ann Plast Surg* 2010; **65**: 411-417 [PMID: 20841993 DOI:

- 10.1097/SAP.0b013e3181e1335b]
- 22 **Nath RK**, Avila MB, Karicherla P. Triangle tilt surgery as salvage procedure for failed shoulder surgery in obstetric brachial plexus injury. *Pediatr Surg Int* 2010; **26**: 913-918 [PMID: 20668864 DOI: 10.1007/s00383-010-2673-7]
 - 23 **Nath RK**, Liu X, Melcher SE, Fan J. Long-term outcomes of triangle tilt surgery for obstetric brachial plexus injury. *Pediatr Surg Int* 2010; **26**: 393-399 [PMID: 20130887 DOI: 10.1007/s00383-010-2550-4]
 - 24 **Nath RK**, Mahmooduddin F. Triangle tilt surgery: effect on coracohumeral distance and external rotation of the glenohumeral joint. *Eplasty* 2010; **10**: e67 [PMID: 21119773]
 - 25 **Nath RK**, Lyons AB, Melcher SE, Paizi M. Surgical correction of the medial rotation contracture in obstetric brachial plexus palsy. *J Bone Joint Surg Br* 2007; **89**: 1638-1644 [PMID: 18057366 DOI: 10.1302/0301-620X.89B12.18757]
 - 26 **Nath RK**, Melcher SE, Paizi M. Surgical correction of unsuccessful derotational humeral osteotomy in obstetric brachial plexus palsy: evidence of the significance of scapular deformity in the pathophysiology of the medial rotation contracture. *J Brachial Plex Peripher Nerve Inj* 2006; **1**: 9 [PMID: 17192183 DOI: 10.1186/1749-7221-1-9]
 - 27 **Nath RK**, Somasundaram C, Mahmooduddin F. Triangle tilt and steel osteotomy: similar approaches to common problems. *Open Orthop J* 2011; **5**: 124-133 [PMID: 21584207 DOI: 10.2174/1874325001105010124]
 - 28 **Nath RK**, Somasundaram C, Melcher SE, Bala M, Wentz MJ. Arm rotated medially with supination - the ARMS variant: description of its surgical correction. *BMC Musculoskelet Disord* 2009; **10**: 32 [PMID: 19291305 DOI: 10.1186/1471-2474-10-32]
 - 29 **Friedman RJ**, Hawthorne KB, Genez BM. The use of computerized tomography in the measurement of glenoid version. *J Bone Joint Surg Am* 1992; **74**: 1032-1037 [PMID: 1522089]
 - 30 **Nath RK**, Paizi M. Scapular deformity in obstetric brachial plexus palsy: a new finding. *Surg Radiol Anat* 2007; **29**: 133-140 [PMID: 17262175 DOI: 10.1007/s00276-006-0173-1]
 - 31 **Nath RK**, Somasundaram C. Successful outcome of modified quad surgical procedure in preteen and teen patients with brachial plexus birth palsy. *Eplasty* 2012; **12**: e54 [PMID: 23308301]
 - 32 **Nath RK**, Kumar N, Somasundaram C. Modified Quad surgery significantly improves the median nerve conduction and functional outcomes in obstetric brachial plexus nerve injury. *Ann Surg Innov Res* 2013; **7**: 5 [PMID: 23714699 DOI: 10.1186/1750-1164-7-5]

P- Reviewer: Anand A, Franklyn M **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Lu YJ



Randomized Controlled Trial

Stochastic resonance whole body vibration increases perceived muscle relaxation but not cardiovascular activation: A randomized controlled trial

Achim Elfering, Christian Burger, Volker Schade, Lorenz Radlinger

Achim Elfering, Christian Burger, Department of Work and Organizational Psychology, University of Bern, 3000 Bern, Switzerland

Volker Schade, Centre for Human Resource Management and Organizational Engineering, 3013 Bern, Switzerland

Lorenz Radlinger, Bern University of Applied Sciences, Health, 3008 Bern, Switzerland

Author contributions: Burger C performed the majority of experiment; Schade V and Radlinger L co-ordinated and provided the collection of data and were also involved in editing the manuscript; Elfering A designed the study, did the analyses and wrote the manuscript.

Supported by the Swiss National Accident Insurance Fund (SUVA, Project “Stochastisches Resonanztraining”) to Achim Elfering, Volker Schade and Lorenz Radlinger.

Institutional review board statement: This study was reviewed and approved by the ethical committee of the responsible University faculty.

Clinical trial registration statement: This study includes no patients and is not registered.

Informed consent statement: All study participants, or their legal guardian, provided informed verbal consent prior to study enrollment.

Conflict-of-interest statement: All author(s) state that for the current paper there is no financial or other relationship that might lead to a conflict of interest. There is no financial or other involvement of any stakeholders.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this

work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Achim Elfering, PhD, Department of Work and Organizational Psychology, University of Bern, Fabrikstrasse 8, 3000 Bern, Switzerland. achim.elfering@psy.unibe.ch
 Telephone: +41-31-6313639

Received: March 9, 2016

Peer-review started: March 15, 2016

First decision: April 20, 2016

Revised: August 18, 2016

Accepted: August 30, 2016

Article in press: August 31, 2016

Published online: November 18, 2016

Abstract

AIM

To investigate the acute effects of stochastic resonance whole body vibration (SR-WBV), including muscle relaxation and cardiovascular activation.

METHODS

Sixty-four healthy students participated. The participants were randomly assigned to sham SR-WBV training at a low intensity (1.5 Hz) or a verum SR-WBV training at a higher intensity (5 Hz). Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and self-reported muscle relaxation were assessed before and immediately after SR-WBV.

RESULTS

Two factorial analyses of variance (ANOVA) showed a significant interaction between pre- vs post-SR-WBV

measurements and SR-WBV conditions for muscle relaxation in the neck and back [$F(1,55) = 3.35$, $P = 0.048$, $\eta^2 = 0.07$]. Muscle relaxation in the neck and back increased in verum SR-WBV, but not in sham SR-WBV. No significant changes between pre- and post-training levels of SBD, DBD and HR were observed either in sham or verum SR-WBV conditions. With verum SR-WBV, improved muscle relaxation was the most significant in participants who reported the experience of back, neck or shoulder pain more than once a month ($P < 0.05$).

CONCLUSION

A single session of SR-WBV increased muscle relaxation in young healthy individuals, while cardiovascular load was low. An increase in musculoskeletal relaxation in the neck and back is a potential mediator of pain reduction in preventive worksite SR-WBV trials.

Key words: Musculoskeletal system; Prevention; Blood pressure; Heart rate; Low back pain

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This randomized controlled trial shows musculoskeletal relaxation to increase after application of a single training of stochastic resonance whole body vibration (SR-WBV). SR-WBV increased muscle relaxation especially in those who suffered from musculoskeletal pain in the last year. Participants reported improved muscular relaxation while the cardiovascular activation as indicated by blood pressure and heart rate was very low. In addition to ergonomic interventions SR-WBV contributes to prevent muscle related pain at work.

Elfering A, Burger C, Schade V, Radlinger L. Stochastic resonance whole body vibration increases perceived muscle relaxation but not cardiovascular activation: A randomized controlled trial. *World J Orthop* 2016; 7(11): 758-765 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/758.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.758>

INTRODUCTION

Whilst evidence for long-lasting vibration exposure at work, as a risk factor for musculoskeletal disease (MSD), is substantial^[1], recent research also showed the beneficial training effects of brief vibration experiences^[2]. It is noteworthy that it is low frequency vibration exposure (5-12 Hz) that is more promising and seems safer than high frequency exposure at 20 to 60 Hz^[3,4]. Stochastic resonance whole body vibration training (SR-WBV) consists of low frequency exposure and has been shown to reduce pain in those with chronic MSD^[5]. The outcome of SR-WBV at the worksite is promising. Four weeks of SR-WBV were reported to increase musculoskeletal well-being in the workers of a steel

manufacturing company^[6], but also in employees that engage in sedentary work, especially those who suffered from back pain prior to SR-WBV^[7]. The latest randomised controlled trial with eight weeks of SR-WBV also showed the positive effects of SR-WBV in the employees of a university hospital, especially in those with baseline health restraints^[8]. In the same population, SR-WBV was also shown to increase posture control, which was assessed by mediolateral sway on a force plate before and after the eight-week trial^[9]. The positive effects of SR-WBV were also shown in the musculoskeletal function of young healthy adults^[10], and one more study confirmed electromyographically that activation of the descending trapezius muscle decreased after SR-WBV, while blood flow and skin temperature also increased in this area, and the energy cost of SR-WBV was low^[11]. A change in back muscle activation from induced SR-WBV training for the sensorimotor system, and not primarily from an increase in fitness, seemed to be involved in the overall positive effects of SR-WBV on musculoskeletal well-being and function^[7]. Therefore, it is a plus of SR-WBV that the self-reported physical demands seemed to be small for most participants, and no sweating was reported. Even so, not only the muscle relaxation that followed the activation of the descending trapezius muscle, but also the change in blood pressure and heart rate from SR-WBV, should be evaluated to estimate the overall demands of SR-WBV training. The current randomized controlled trial tests the hypothesis that 5Hz-SR-WBV improves muscle relaxation (H1), and that 5Hz-SR-WBV triggers cardiovascular activation (H2), whereas 1.5 Hz-SR-WBV (sham condition) has no effect on muscle relaxation or cardiovascular activation. Therefore, 5 Hz-SR-WBV should have the greatest effect on muscle relaxation in those who reported back, neck or shoulder pain in last 12 mo (H3). The test of the second hypothesis is essential. Minimal cardiovascular activation would allow individuals at modest cardiovascular risk to perform SR-WBV.

How SR-WBV works

SR-WBV benefits from the effects of stochastic resonance by applying vibrations of low frequency with a maximal degree of complexity and unpredictability. Ward and colleagues defined stochastic resonance as "a nonlinear cooperative effect wherein the addition of a random process, or 'noise' to a weak signal, or stimulus results in improved detectability or enhanced information content in some response"^[12]. SR-WBV differs completely from simple frequency fast sinusoidal vibrations, like the ones applied by the most common and conventional sinusoidal vibration training devices. During SR-WBV, the human body cannot anticipate the upcoming vibration movements, and therefore, the body is constantly challenged to adapt its neural and muscular reactions and shows no muscular fatigue during the application^[13-16]. SR-WBV seems to provoke an interaction of different types of neurophysiologic sensors and the

adjustment of afferent and efferent signals, which probably acts as exercise for the sensorimotor system^[13]. The observed increase in strength is mainly attributed to neural adaptation, which leads to improved inter- and intramuscular coordination, which, in turn, allows the increased activation of prime movers in specific movements, and better coordination in the activation of all relevant muscles^[17] or a higher muscular activity in insufficient muscles, when compared to sinusoidal vibration^[18]. A low risk of injury and only the rare manifestation of side-effects make SR-WBV an attractive preventive intervention^[5,19].



Figure 1 Starting position on stochastic resonance whole body vibration device.

MATERIALS AND METHODS

Ethics

The study was performed in consensus with all requirement defined by the Swiss Society of Psychology. The study was conducted with the understanding and the consent of the human subject. The Ethical Committee of the responsible University faculty has approved the study.

Participants

Expecting a moderate effect size for the repeated measures, within-between interaction and a requirement of a 90% power to detect an existing difference, the required sample size was 64 participants. Sixty-four undergraduate and graduate students were asked for participation and all agreed to participate (34 female and 30 male psychology majors, mean age = 27.6 years, SD = 5.0 years). The inclusion criterion was acute health status. The exclusion criteria for participation were recorded anamnestically, and comprised acute, past or chronic arthropathologies, troubles in the cardiovascular system, psychopathology, spondylolysis, spondylolisthesis, tumors, disc prolapse with neurological failure, rheumatism, articular gout, osteoporosis, activated arthritis with inflammatory signs, stage 4 arthritis, fever, cold, etc. No participant had to be excluded from the study. All participants finished the study protocol.

Procedure

The study was conducted at a University facility. The participants completed a single SR-WBV training session. A special device was applied for SR-WBV (©Zeptor med plus Noise, FreiSwiss AG, Zurich, Switzerland). Its key features were two independently and one-dimensional (up/down) stochastically oscillating floorboards, with two passive degrees of freedom (forward/backward and right/left). Each SR-WBV session was supervised, and the participants were instructed to stand in an upright position on the footboards with their arms hanging loose to the side and with slightly bent knees and hips (Figure 1). Both legs should have contact to the plates. It was permitted to change the knee angle but participants were instructed not to stand up straight because in that position vibration is conducted to the head. Figure 1

was shown to demonstrate the posture to participants. The participants were randomly allocated to SR-WBV groups (5 Hz verum condition or 1.5 Hz sham condition). The randomisation was based on the use of a list of random numbers^[20]. The session consisted of three series of SR-WBV, which lasted one minute each, with a one-minute break between them. The 5 Hz verum condition was used as the minimum effective SR-WBV stimulation loading parameter, while the 1.5 Hz sham condition can be expected to have no training effect^[10,21]. Participants were blind with respect to their training frequency condition. The investigator did the setting of the frequency before the training session started. The setting-screen was additionally covered by a piece of paper so that the participants never knew the exact vibration frequency.

Blood pressure and heart rate

The blood pressure cuff was put into place at the beginning of the session before the participants filled out the questionnaire. Participants wore the ambulatory blood pressure device (blood pressure monitor Spacelabs © model 90207; readings taken by the Korotkoff method) throughout the experimental session. Blood pressure was recorded one minute before and after the SR-WBV session. In an ambulatory blood pressure assessment, the Spacelabs 90207 often is denoted as the "gold standard"^[22]. To ensure the comparability of blood pressure levels measured during the presentations, all analyses are based on data recorded in a sitting position.

Muscular pain and relaxation assessment

Musculoskeletal pain was assessed with a question that addressed musculoskeletal pain in the back or neck/shoulders in the last 12 mo (never, less than monthly, less than weekly, less than daily, daily). It is part of a scale that measures psychosomatic complaints that was developed by Mohr *et al.*^[23] based on the previous work of Fahrenberg *et al.*^[24]. Muscular relaxation was assessed by a short version of the self-administered questionnaire of Burger *et al.*^[6] that was completed

Table 1 Mean values of study variables in verum stochastic resonance whole body vibration and sham stochastic resonance whole body vibration groups

Variable	Verum-SR-WBV (5 Hz SR-WBV) (n = 34)		Sham SR-WBV (1.5 Hz SR-WBV) (n = 30)		t	P
	Mean	SD	Mean	SD		
Systolic blood pressure						
Pre-training	129.67	12.78	120.9	9.68	3.05	0.003
Post-training	126.97	11.54	120.57	10.43	2.32	0.024
Diastolic blood pressure						
Pre-training	78.61	11.00	75.27	7.64	1.39	0.171
Post-training	79.00	8.92	75.13	8.37	1.78	0.080
Heart rate						
Pre-training	71.09	12.03	69.1	15.67	0.57	0.572
Post-training	69.94	11.51	68.4	13.25	0.50	0.620
Muscle relaxation						
Pre-training	6.47	2.06	6.87	2.47	0.70	0.488
Post-training	7.00	2.10	6.7	2.59	0.51	0.611
Age (yr)	27.76	3.70	27.4	6.15	0.28	0.779 ¹
Sex	18 f, 16 m		16 f, 14 m		$\chi^2 = 0.001$	0.975
BMI	22.58	2.59	21.68	2.80	1.34	0.187
Fitness	3.65	0.65	3.66	0.72	-0.05	0.963
Smoker (10 cigarettes or more)	12 (6)		7 (3)		$\chi^2 = 1.09$	0.296
Smoking (cigarettes)	3.53	6.33	2.30	6.98	0.74	0.463
Cups of coffee before training	1.50	1.11	1.67	1.47	-0.52	0.608
Back, neck or shoulder pain in last 12 mo	2.71	1.00	2.63	1.40	0.24	0.815 ¹

¹Corrected for unequal variances. BMI: Body mass index; SR-WBV: Stochastic resonance whole body vibration; f: Female; m: Male.

before and after SR-WBV. The participants were asked to rate muscle relaxation on a 10-point Likert scale. The question was introduced, "At the moment, how do you rate your personal sensation in your muscles and joints (back, shoulder and neck, leg muscles, etc.)?", which was followed by "Relaxation in the muscles and joints", and the corresponding 10-point rating scale from "no relaxation" to "strongest imaginable relaxation".

Statistical analysis

Self-reported muscle relaxation, systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were analysed in a two-factorial ANOVA, including the repeated measurement (pre- vs post-session measurement) of SBP, DBP, HR and self-reported muscle relaxation as a within-subjects factor, and the SR-WBV training group condition (verum: 5 Hz, sham: 1.5 Hz) as a between factor.

We tested hypothesis 3 - expected gain in muscle relaxation to be the largest in verum SR-WBV and among those with musculoskeletal pain, compared with verum SR-WBV with no pain, and sham SR-WBV with and without pain - by planned contrasts as recommended by Strube *et al.*^[25]. The change in muscle relaxation (post-SR-WBV minus pre-SR-WBV) was the dependent variable. *P*-values were two-tailed with α set to 5%.

RESULTS

Participant characteristics

Before the training study started, the participants reported the frequency of musculoskeletal pain episodes in the

back, neck or shoulders in the last 12 mo. Thirteen participants (20.3%) reported that they had never experienced pain during this period of time. Fifteen participants (23.4%) reported pain episodes less than monthly, and 21 participants (32.8%) reported pain episodes less than weekly. Ten participants (15.6%) reported pain episodes that occurred every week, but less than daily. Five participants (7.8%) experienced pain every day in the last 12 mo. Sixty-four healthy students participated in this study. Table 1 depicts the descriptive study results. The 64 participants were randomly assigned to SR-WBV conditions, and no significant differences in musculoskeletal pain episodes in the back, neck or shoulders in the last 12 mo were observed between the groups of verum SR-WBV and sham SR-WBV (Table 1). Thirty-four participants were assigned to verum SR-WBV, and 30 participants were assigned to sham-SR-WBV. The verum and sham SR-WBV groups did not differ significantly in any demographic characteristics or in baseline muscle relaxation or DBP and HR. However, the baseline and follow-up SBP was significantly higher in verum SR-WBV than in sham SR-WBV (Table 1). Table 2 shows the correlations between study variables. Pain episodes in the back, neck or shoulders in the last 12 mo were negatively related to sex, showing higher pain in women than in men. Fitness was negatively related to pain episodes in the back, neck or shoulders.

SR-WBV and improved muscle relaxation (H1)

The ANOVA results for the test of the first hypothesis are shown in Table 3. A significant interaction term indicated that verum SR-WBV improved muscle relaxation, while

Table 2 Correlations between study variables

Variables	SR-WBV condition	SBP pre	SBP post	DBP pre	DBP post	HR pre	HR post	Relax pre	Relax post	Age	Sex	BMI	Fitness	Smoking	Coffee
SR-WBV Condition															
SBP pre	-0.36 ^c														
SBP post	-0.28 ^a	0.83 ^c													
DBP pre	-0.18	0.63 ^c	0.57 ^c												
DBP post	-0.22	0.59 ^e	0.71 ^e	0.68 ^c											
HR pre	-0.07	0.02	0.01	0.22	0.22										
HR post	-0.06	0.03	0.07	0.21	0.24	0.76 ^c									
Relaxation pre	0.09	0.02	0.22	-0.04	0.01	0.04	-0.01								
Relaxation post	-0.07	0.09	0.24	0.03	0.03	0.01	-0.04	0.84 ^a							
Age	-0.04	0.36 ^c	0.40 ^c	0.24	0.23	-0.03	-0.11	0.26 ^a	0.26 ^a						
Sex	-0.01	0.26 ^a	0.36 ^c	-0.07	0.05	-0.16	-0.1	0.28 ^a	0.15	0.29 ^a					
BMI	-0.17	0.08	0.14	-0.14	0	-0.32 ^c	-0.19	-0.01	0.02	0.15	0.45 ^f				
Fitness	0.01	0.15	0.19	-0.13	-0.2	-0.19	-0.16	0.41 ^c	0.38 ^c	0.30 ^a	0.34 ^c	0.24			
Smoking (number of cigarettes)	-0.09	0.10	0.07	-0.12	0.06	0.25 ^a	0.37 ^c	-0.01	-0.07	0.07	0.36 ^c	0.28 ^a	-0.02		
Cups of coffee before training	0.07	0.09	0.01	-0.01	0.01	0.07	0.16	-0.28 ^a	-0.28 ^a	0.20	0.16	0.16	-0.18	0.33 ^c	
Back, neck or shoulder pain in last 12 mo	-0.03	-0.18	-0.30 ^a	-0.04	-0.14	-0.08	0.03	-0.55 ^c	-0.59 ^e	-0.09	-0.27 ^a	0.02	-0.26 ^a	-0.03	0.24

^a*P* < 0.05, ^c*P* < 0.01, ^e*P* < 0.001: Correlations coefficients that significantly differ from zero. SR-WBV: Stochastic resonance whole body vibration; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate.

Table 3 Results of two-factorial ANOVA

	Sum of squares	df	Mean square	F	P	Partial eta-square
Inner-subject effects						
Pre- vs post-training (<i>n</i> = 64)	1.05	1	1.05	1.32	0.255	0.021
Training group (5 Hz vs 1.5 Hz)	3.86	1	3.86	4.85	0.031	0.073
Within subjects error	49.32	62	0.80			
Between subjects effects						
Constant	8.91	1	8.91	1.18	0.282	0.021
Training group (5 Hz vs 1.5 Hz)	0.74	1	0.74	0.01	0.931	0.000
Between subjects error	608.92	62	9.82			

no change appeared in sham SR-WBV [$F(1,62) = 3.86, P = 0.031, \eta^2 = 0.069$]. Figure 2 shows the change in muscle relaxation in both study groups.

SR-WBV and increase in cardiovascular activation (H2)

In verum and sham SR-WBV, the mean levels in SBP, DBP and HR were almost the same before and after SR-WBV (Table 1). The ANOVAs of SBP, DBP and HR did not show significant interaction effects [SBP: $F(1,61) = 1.92, P = 0.171, \eta^2 = 0.030$; DBP: $F(1,61) = 0.07, P = 0.792, \eta^2 = 0.001$; HR: $F(1,61) = 0.010, P = 0.919, \eta^2 = 0$].

SR-WBV and back, neck or shoulder pain in last 12 mo (H3)

Verum SR-WBV was expected to have the greatest effects on muscle relaxation in those who reported back, neck or shoulder pain in last 12 mo. These individuals should benefit more from 5Hz SR-WBV than those without pain and those with and without pain in the

sham SR-WBV condition. Figure 3 shows the change in the musculoskeletal relaxation for SR-WBV groups separately, for those with and without back, neck or shoulder pain in last 12 mo. As expected, the increase in muscle relaxation was the greatest in those with pain in the verum SR-WBV group, and was significantly greater than in all other groups, as shown in the planned contrast analysis [$F(1,60) = 5.30, P = 0.025, \eta^2 = 0.081$].

DISCUSSION

The current findings showed self-reported musculoskeletal relaxation increased significantly after verum SR-WBV, but not after sham SR-WBV, while SBP, DBP and HR did not change in either verum SR-WBV or sham SR-WBV. The current results confirm a recent more explorative investigation on acute effects of SR-WBV that showed increased muscle relaxation measured by electromyography and low cardiac activation measured by heart rate variability^[11]. Confirmation was important

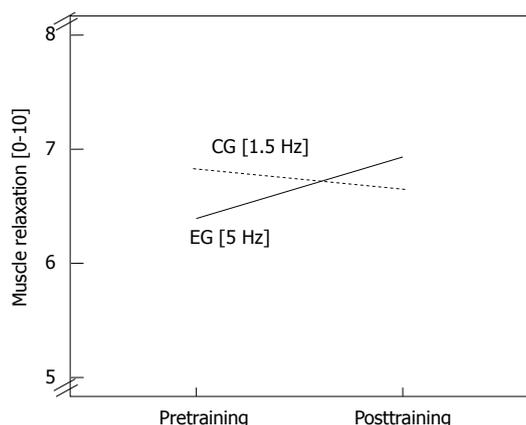


Figure 2 Self-reported muscle relaxation before and after stochastic resonance whole body vibration.

because the previous investigation was based on a comparably small sample (one third of the sample size of the current study) and was based solely on a repeated measurements design^[11]. Hence, the current randomized controlled trial increased the evidence that one trial of SR-WBV has beneficial musculoskeletal effects while cardiovascular load is moderate. Muscle relaxation after SR-WBV prevents musculoskeletal pain that may arise from consistently high muscle tension^[1]. Repeated SR-WBV may decrease muscle tension and musculoskeletal pain. The present findings showed that participants who reported back, neck and shoulder pain episodes in the last 12 mo were the main beneficiaries of the overall positive effects of SR-WBV on muscle relaxation. Using repeated SR-WBV Elfering and colleagues found in a four-week worksite study that SR-WBV was more clearly linked to reduced pain in those who suffered from musculoskeletal pain prior to training, while those who were pain-free benefited less^[15]. Thus, SR-WBV seems to have specific positive effects on the neuro-muscular system, while the absence of cardiovascular activation indicates that the positive effects are unlikely to be mediated by changes in overall fitness.

Four and eight-week worksite training studies showed SR-WBV can easily be done before, during or after work without having to change clothes or take a shower afterwards^[6-9]. Further, the low cardiovascular demands of SR-WBV make SR-WBV a safe worksite prevention tool.

Even so, the beneficial effects of SR-WBV seem to contradict evidence of the harmful effects of vibration exposure at work^[1]. However, a distinction should be made between SR-WBV and harmful vibration at work^[26]. The damaging effects of vibration at work are caused by chronic exposure - with long exposure and short rest cycles - to a rather regular vibration that is often oscillating at a large amplitude or at frequencies of mechanical resonance^[27]. In contrast, SR-WBV training efficiency and its therapeutic effects were summarised

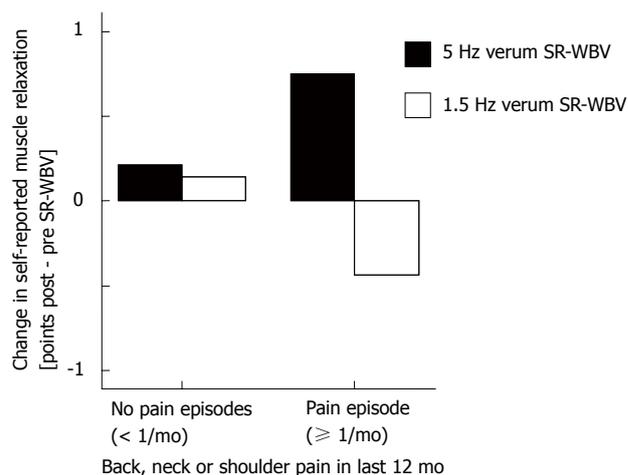


Figure 3 Change in self-reported muscle relaxation by stochastic resonance whole body vibration and back, neck or shoulder pain in last 12 mo before stochastic resonance whole body vibration.

recently^[5,27]. SR-WBV may have risks and benefits, and both should be studied. A review of 112 studies on whole body vibration reported very few side effects (0.00120% in 104 studies that used sinus whole body vibration, and 0.00069% in eight studies that used SR-WBV)^[19]. More serious side effects have been exclusively found in studies that used sinusoidal whole body vibration, but not in studies that used SR-WBV^[19]. SR-WBV seems to be a safe training intervention with usually harmless adverse effects when a careful evaluation of the medical history is performed before SR-WBV to evaluate contraindications or the potential risk factors of the subjects. In addition, one should avoid unnecessarily intense exposure to keep the risk of side-effects as low as possible. Therefore, we did 60-s trainings, which is the shortest period known to have a training effect. The next step in the evaluation should test worksite SR-WBV to reduce MSD, but it should also include an economic evaluation^[28].

This study had an experimental design, and many potential confounders were controlled by randomisation. However, unexpectedly, baseline differences in SBP were observed between the SR-WBV groups, with higher SBP levels in verum SR-WBV. Thus, a regression to mean levels cannot be excluded in SBP measurement after SR-WBV. This is noteworthy; because of frequent measurement artefacts, SBP and DBP could only be measured after SR-WBV and not during SR-WBV. The participants were blind with respect to their verum vs sham SR-WBV condition. However, a blinding of the primary investigator was not feasible.

The participants benefited from low frequency 5 Hz SR-WBV after three one-minute trials within one 10-min training session. The participants with a frequent experience of back, neck and shoulder in last 12 mo had improved muscular relaxation after SR-WBV, whilst blood pressure levels and heart rate were nearly unchanged by SR-WBV. In addition to ergonomic intervention, training and participatory work redesign SR-WBV may help to

prevent and reduce MSD at work.

COMMENTS

Background

Musculoskeletal pain is common and so far no experiment tested the acute effects of a single stochastic resonance whole-body vibration training (SR-WBV) on muscle relaxation and blood pressure.

Research frontiers

There is need for research on short, economic, and effective training intervention. In this experiment, author(s) showed a single short SR-WBV training to increase musculoskeletal relaxation.

Innovations and breakthroughs

The experiment showed benefits were higher in those with experience of musculoskeletal pain while cardiovascular activation was low.

Applications

In previous works including 4 or even 8 wk of SR-WBV was found to improve musculoskeletal pain and body balance, measured as self-report and as recorded body sway on a balance platform. Improved body balance is connected to a lower risk of slips and falls. Short trials of SR-WBV that amount to less than 10 min can be done at a worksite without a change of clothes or shoes. Cardiovascular demand with 5 Hz SR-WBV is low and permits SR-WBV in the untrained or elderly workforce.

Terminology

SR-WBV constantly challenges the neuromusculoskeletal coordination to adapt to unforeseeable change.

Peer-review

This is an interesting investigation and the authors are experts in stochastic resonance whole body vibration.

REFERENCES

- 1 Elfering A, Mannion AF. Epidemiology and risk factors of spinal disorders. In: Boos N, Aebi M. *Spinal disorders - Fundamentals of diagnosis and treatment*. Berlin: Springer, 2008: 153-173 [DOI: 10.1007/978-3-540-69091-7_6]
- 2 Rogan S, Hilfiker R, Herren K, Radlinger L, de Bruin ED. Effects of whole-body vibration on postural control in elderly: a systematic review and meta-analysis. *BMC Geriatr* 2011; **11**: 72 [PMID: 22054046 DOI: 10.1186/1471-2318-11-72]
- 3 Herren K, Hotz Hngtner C, Oberli A, Radlinger L. Cardiovascular and metabolic strain during stochastic resonance therapy in stroke patients. *Physioscience* 2009; **5**: 13-17 [DOI: 10.1055/s-0028-1109140]
- 4 Rittweger J. Vibration as an exercise modality: how it may work, and what its potential might be. *Eur J Appl Physiol* 2010; **108**: 877-904 [PMID: 20012646 DOI: 10.1007/s00421-009-1303-3]
- 5 Pang MY. Whole body vibration therapy in fracture prevention among adults with chronic disease. *World J Orthop* 2010; **1**: 20-25 [PMID: 22474623 DOI: 10.5312/wjo.v1.i1.20]
- 6 Burger C, Schade V, Lindner C, Radlinger L, Elfering A. Stochastic resonance training reduces musculoskeletal symptoms in metal manufacturing workers: a controlled preventive intervention study. *Work* 2012; **42**: 269-278 [PMID: 22699194 DOI: 10.3233/WOR-2012-1350]
- 7 Elfering A, Arnold S, Schade V, Burger C, Radlinger L. Stochastic resonance whole-body vibration, musculoskeletal symptoms, and body balance: a worksite training study. *Saf Health Work* 2013; **4**: 149-155 [PMID: 24106645 DOI: 10.1016/j.shaw.2013.07.002]
- 8 Elfering A, Schade V, Burger C, Stcklin L, Baur S, Radlinger L. Stochastic resonance training at work reduces musculoskeletal pain in nurses. In: Duffy V, Lightner N. *Advances in Human Aspects of Healthcare*. USA: AHFE Conference, 305-314. Available from: URL: <http://boris.unibe.ch/65745/>
- 9 Elfering A, Schade V, Stoecklin L, Baur S, Burger C, Radlinger L. Stochastic resonance whole-body vibration improves postural control in health care professionals: a worksite randomized controlled trial. *Workplace Health Saf* 2014; **62**: 187-196 [PMID: 24806038 DOI: 10.3928/21650799-20140422-04]
- 10 Elfering A, Thomann J, Schade V, Radlinger L. Stochastic resonance whole body vibration reduces musculoskeletal pain: A randomized controlled trial. *World J Orthop* 2011; **2**: 116-120 [PMID: 22474630 DOI: 10.5312/wjo.v2.i12.116]
- 11 Elfering A, Zahno J, Taeymans J, Blasimann A, Radlinger L. Acute effects of stochastic resonance whole body vibration. *World J Orthop* 2013; **4**: 291-298 [PMID: 24147265 DOI: 10.5312/wjo.v4.i4.291]
- 12 Ward LM, Neiman A, Moss F. Stochastic resonance in psychophysics and in animal behavior. *Biol Cybern* 2002; **87**: 91-101 [PMID: 12181585 DOI: 10.1007/s00422-002-0328-z]
- 13 Haas CT, Turbanski S, Kessler K, Schmidtbleicher D. The effects of random whole-body-vibration on motor symptoms in Parkinson's disease. *NeuroRehabilitation* 2006; **21**: 29-36 [PMID: 16720935]
- 14 Luginbuehl H, Lehmann C, Gerber R, Kuhn A, Hilfiker R, Baeyens JP, Radlinger L. Continuous versus intermittent stochastic resonance whole body vibration and its effect on pelvic floor muscle activity. *NeuroUrol Urodyn* 2012; **31**: 683-687 [PMID: 22395850 DOI: 10.1002/nau.21251]
- 15 Ross SE, Arnold BL, Blackburn JT, Brown CN, Guskiewicz KM. Enhanced balance associated with coordination training with stochastic resonance stimulation in subjects with functional ankle instability: an experimental trial. *J Neuroeng Rehabil* 2007; **4**: 47 [PMID: 18086314 DOI: 10.1186/1743-0003-4-47]
- 16 Schollhorn WI, Beckmann H, Michelbrink M, Sechelmann M, Trockel M, Davids K. Does noise provide a basis for the unification of motor learning theories? *Int J Sport Psychol* 2006; **37**: 1-22
- 17 Haas CT, Turbanski S, Kaiser I, Schmidtbleicher D. Biomechanical and physiological effects of oscillating mechanical stimuli in humans. *Deutsche Zeitschrift fr Sportmedizin* 2004; **55**: 34-42
- 18 Lauper M, Kuhn A, Gerber R, Luginbühl H, Radlinger L. Pelvic floor stimulation: what are the good vibrations? *NeuroUrol Urodyn* 2009; **28**: 405-410 [PMID: 19283866 DOI: 10.1002/nau.20669]
- 19 Herren K, Radlinger L. Risks and side-effects of whole-body vibration training. Special Interest Report Poster WCPT Congress Amsterdam 2011 (Number: SI-PO-201-21-Tue). *Physiotherapy* 2011; **97** Supplement: S1
- 20 Yaremko RM, Harari H, Harrison RC, Lynn E. *Reference handbook on research and statistical methods in psychology*. New York: Harper & Row, 1982: 1-366
- 21 Madou KH, Cronin JB. The effects of whole body vibration on physical and physiological capability in special populations. *Hong Kong Physio J* 2008; **26**: 24-38 [DOI: 10.1016/S10137025(09)70005-3]
- 22 Magometschnigg D, Mair N, Hitzzenberger G. NAIS-284 blood pressure watch in comparison to SpaceLabs 90207 - precision and reliability. *J Hyperton* 2001; **5**: 16-22
- 23 Mohr G. Die Erfassung psychischer Befindensbeeinträchtigung bei Industriearbeitern [Assessment of strain in industrial workers]. Frankfurt: Lang, 1986: 1-353
- 24 Fahrenberg J. Die Freiburger Beschwerdeliste FBL [The Freiburg Symptom list]. *Z Klin Psychol Psychoth* 1975; **4**: 49-100
- 25 Strube MJ, Bobko P. Testing hypotheses about ordinal interactions: Simulations and further comments. *J Appl Psychol* 1989; **74**: 247-252 [DOI: 10.1037/0021-9010.74.2.247]
- 26 Griffin MJ. *Handbook of human vibration*. San Diego: Academic Press, 1996: 1-998
- 27 Haas CT. Vibrationstraining, biomechanische Stimulation und stochastische Resonanztherapie [Vibration training, biomechanical stimulation and stochastic resonance therapy]. *pt_Zeitschrift fr*

Physiotherapeuten 2008; **60**: 728-740. Available from: URL: http://www.wellwave.net/page4/downloads-2/files/Review_08_Stochastic_Haas.pdf

28 **Ramos DG**, Arezes PM, Afonso P. Economic evaluation of occupational safety preventive measures in a hospital. *Work* 2015; **51**: 495-504 [PMID: 24939111 DOI: 10.3233/WOR-141884]

P- Reviewer: Hernandez-Sanchez S, Paschalis V **S- Editor:** Kong JX
L- Editor: A **E- Editor:** Lu YJ



Spinal gout: A review with case illustration

Hossein Elgafy, Xiaochen Liu, Joseph Herron

Hossein Elgafy, Xiaochen Liu, Joseph Herron, Department of Orthopedics, University of Toledo Medical Center, Toledo, OH 43614-5807, United States

Author contributions: All the authors contributed in outlining the manuscript, gathering the data, and writing the manuscript.

Conflict-of-interest statement: None of the authors have any financial or other conflicts of interest that may bias the current study.

Data sharing statement: The technical appendix, statistical code, and dataset are available from the corresponding author at hossein.elgafy@utoledo.edu.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Hossein Elgafy, MD, MCH, FRCSEd, FRCSC, Department of Orthopedics, University of Toledo Medical Center, 3065 Arlington Avenue, Toledo, OH 43614-5807, United States. hkelgafy@aol.com
 Telephone: +1-419-3833515
 Fax: +1-419-3833526

Received: April 27, 2016
 Peer-review started: April 28, 2016
 First decision: July 6, 2016
 Revised: August 1, 2016
 Accepted: August 17, 2016
 Article in press: August 18, 2016
 Published online: November 18, 2016

Abstract

AIM

To summarize clinical presentations and treatment options

of spinal gout in the literature from 2000 to 2014, and present theories for possible mechanism of spinal gout formation.

METHODS

The authors reviewed 68 published cases of spinal gout, which were collected by searching "spinal gout" on PubMed from 2000 to 2014. The data were analyzed for clinical features, anatomical location of spinal gout, laboratory studies, imaging studies, and treatment choices.

RESULTS

Of the 68 patients reviewed, the most common clinical presentation was back or neck pain in 69.1% of patients. The most common laboratory study was elevated uric acid levels in 66.2% of patients. The most common diagnostic image finding was hypointense lesion of the gout tophi on the T1-weighted magnetic resonance imaging scan. The most common surgical treatment performed was a laminectomy in 51.5% and non-surgical treatment was performed in 29.4% of patients.

CONCLUSION

Spinal gout most commonly present as back or neck pain with majority of reported patients with elevated uric acid. The diagnosis of spinal gout is confirmed with the presence of negatively birefringent monosodium urate crystals in tissue. Treatment for spinal gout involves medication for the reduction of uric acid level and surgery if patient symptoms failed to respond to medical treatment.

Key words: Spinal; Gout; Tophi; Monosodium urate

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Gout is a common inflammatory arthritis that rarely affects the spine. In such cases, patients may experience back pain, myelopathic symptoms and radiculopathy. Clinical findings are non-specific. Therefore, it is necessary to have an awareness of the diagnosis,

especially in patients with a clinical history of gout and/or elevated inflammatory markers and hyperuricemia. While magnetic resonance imaging is the major non-invasive diagnostic method, all suspicious findings on imaging require surgical sampling for pathological confirmation. While typical uric acid lowering medications are first-line therapy, cord compression or continued symptoms may necessitate operative intervention if medications fail.

Elgafy H, Liu X, Herron J. Spinal gout: A review with case illustration. *World J Orthop* 2016; 7(11): 766-775 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i11/766.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i11.766>

INTRODUCTION

Gout is a common inflammatory arthritis with an increase in prevalence over the last 20 years. It currently affects over 8 million Americans. The clinical presentation of gout depends on the site of monosodium urate (MSU) crystals precipitation and the subsequent inflammatory response that ensues in the synovial joints and soft tissues. Gout usually manifests as a monoarticular arthritis in the lower extremities. If untreated, nodular masses of MSU crystals called tophi may eventually deposit in extraarticular locations, such as, the axial skeleton. Although traditionally thought of as a rare complication, recent study suggests that axial gout may be more prevalent than suspected^[1]. Gout affecting the spinal column will typically present with neurological compromise, localized pain, and lytic vertebral lesions^[2,3]. Spinal gout can affect the facet joint, laminae, ligamentum flavum, as well as the epidural space^[4].

From 2000 to 2014, approximately 68 case reports have been published on spinal gout. The current manuscript summarizes the most common presenting features, imaging findings, and treatment choices based on the 68 published cases. A case is also presented to provide illustration on the topic.

MATERIALS AND METHODS

Literature review

A PubMed literature search using the key words spinal gout, from January 2000 to December 2014, limited to human studies and restricted to English language literature resulted in 221 publications. Abstracts and articles were then reviewed for content. Articles kept for review included patients who underwent treatment for spinal gout. Furthermore, data required for inclusion in the study included: Patient demographics, clinical presentation, laboratory findings, imaging studies, and treatment methods were collected (Table 1). Articles excluded from the study were those that did not have patients diagnosed with spinal gout and those that did not include patient demographics, clinical presentation,

laboratory findings, imaging studies, and treatment methods. After review, a total of 54 peer reviewed articles met the above criteria and were included for data collection.

RESULTS

The 54 articles accounted for 68 cases of spinal gout with 51 (75%) males and 17 (25%) females and an average age of 59.2 years, 41(60.3%) had prior history of peripheral gout (Table 1).

Clinical presentations

Of the 68 spinal gout patients reviewed, 47 (69.1%) presented with localized back/neck pain, 38 (55.9%) with some form of spinal cord compression, defined as weakness, numbness, loss of bladder or bowel control, and decreased sensation below the compression level, 17 (25%) with spinal nerve root compression or radiculopathy, defined as motor dysfunction or dysesthesia along the course of a specific nerve caused by compression of its root, 13 (19.1%) with fever, 1 (1.5%) with cranial nerve palsy, and 2 (3.0%) with atlanto-axial subluxation (Table 2). Furthermore, among the sites of involvement in the 68 spinal gout patients, 38 (55.9%) were located in the lumbar region, 15 (22.1%) in the thoracic region, 15 (22.1%) in the cervical region, and 1 (1.4%) in an unspecified region (Table 3). One patient demonstrated soft tissue nodularity consistent with gouty tophi on biopsy in both the thoracic and lumbar spinal segments.

Laboratory studies

Laboratory studies of the 68 recorded cases showed 45 (66.2%) with elevated uric acid level at the time of diagnoses, 17 (25%) had elevated erythrocyte sedimentation rates (ESR), 19 (27.9%) had increased C-reactive proteins (CRP) level, 11 (16.2%) had renal insufficiency, 9 (13.2%) had leukocytosis, and 5 (7.4%) had anemia (Table 4).

Imaging studies

On the T1-weighted magnetic resonance imaging (MRI) images, 28 (41.2%) did not report findings, 31 (45.5%) were hypointense, 8 (11.8%) were isointense, and 1 (1.5%) was heterointense. On T2-weighted images, 24 (35.3%) did not report findings, 18 (26.5%) were hypointense, 12 (17.6%) were heterointense, 11 (16.2%) were hyperintense, and 4 (5.9%) were isointense. A gadolinium (Gd)-enhanced MRI scan was obtained from 32 (47.1%) patients. These findings are referenced in (Table 5).

Thirty-seven cases (54.4%) did not report X-ray findings, 12 (17.6%) showed spondylosis or spondylolisthesis, 8 (11.8%) showed bony erosion, 6 (8.8%) were unremarkable, and 5 (7.4%) showed degenerative changes. In addition, 35 (51.5%) did not report computed tomography (CT) findings, 13 (19.1%) showed bony erosion and high density attenuation, 13 (19.1%)

Table 1 List of patient cases of spinal gout in the literature since 2000

No.	Year	Ref.	Age/ sex	Site	Sx/Signs	Duration	Hx Gout	Tophi	Relevant Hx	Hi Urate	MRI T1	T2	Gad	Tx
1	2000	Kao <i>et al</i> ^[5]	82 M	T10-T11	LE weakness	1 mo	Y	NA	NA	Y	Iso	Hypo	NA	T9-T11 lamina
2	2000	Mekelburg <i>et al</i> ^[6]	60 M	L2-3	Back pain	5 mo	Y	NA	NA	Y	NA	NA	NA	Cervical lamina
3	2000	Paquette <i>et al</i> ^[7]	56 M	L3	Back pain, radicular pain	6 yr	N	NA	Arthritis	NA	NA	Hypo	NA	Surgery
4	2000	Thornton <i>et al</i> ^[8]	27 M	L3-L4	Back pain	1 d	Y	NA	RT	Y	Hypo	NA	Y	Medical NOS
5	2001	Barrett <i>et al</i> ^[9]	70 M	L5-S1	Back pain, radicular pain, fever	2 d	Y	NA	RI	N	NA	Hyper	Y	Lamina
6	2001	St George <i>et al</i> ^[10]	60 M	T1-T2	LE weakness, BBD	6 wk	Y	N	NA	NA	NA	Hypo	NA	T1-T2 lamina
7	2001	Wang <i>et al</i> ^[11]	28 M	T9-T10	LE weakness	1 d	Y	N	NA	NA	NA	NA	NA	T9-T10 lamina
8	2002	Hsu <i>et al</i> ^[12]	72 M	L4-S1	Back pain, radicular pain	18 mo	Y	NA	NA	Y	Hypo	Hyper	Y	Lamina
9	2002	Hsu <i>et al</i> ^[12]	77 M	L3-L5	Back pain, radicular pain	12 mo	N	NA	NA	Y	Hypo	Hypo	Y	Lumbar lamina
10	2002	Hsu <i>et al</i> ^[12]	83 M	T9-T11	LE weakness	1 mo	Y	NA	NA	N	Hypo	Hypo	Y	Lamina
11	2002	Hsu <i>et al</i> ^[12]	27 M	L2-S1	Back pain	6 mo	Y	NA	NA	Y	Hypo	Hyper	Y	Medical NOS
12	2002	Souza <i>et al</i> ^[13]	49 M	T9-T10	Back pain, LE weakness	6 mo	Y	NA	NA	NA	Iso	Hypo	Y	T9-T11 lamina
13	2002	Yen <i>et al</i> ^[14]	68 M	C4-C5	Quadripareisis	2 wk	Y	NA	RI	Y	Hypo	Hypo	NA	Surgery
14	2003	Diaz <i>et al</i> ^[15]	74 M	C4-C5	Quadripareisis	1 wk	Y	Y	NA	Y	NA	NA	NA	C4-C5 lamina
15	2004	Draganescu <i>et al</i> ^[16]	48 F	L4	Radicular pain	1 d	Y	Y	Diuretic	Y	NA	Hetero	Y	L4-L5 lamina
16	2004	El Sandid <i>et al</i> ^[17]	32 M	T7-T9	Back pain, fever	Acute	Y	NA	NA	Y	NA	NA	NA	Lamina
17	2004	Nakajima <i>et al</i> ^[18]	39 M	L4-5	Low back pain	NA	Y	Y	Arthritis	Y	NA	NA	Y	Medical
18	2005	Beier <i>et al</i> ^[19]	29 M	L4-L5	Back pain, L5 radiculopathy	Acute	N	N	NA	Y	NA	NA	NA	L4-L5 lamina
19	2005	Celik <i>et al</i> ^[20]	48 M	C1-C2	Neck pain, radiculopathy, paresthesias	2 mo	N	Y	Alcohol	Y	Hypo	Hyper	Y	Medical NOS
20	2005	Chang ^[21]	60 M	L3-L4	B/L L4 radiculopathy	NA	Y	NA	NA	Y	Hypo	Hypo	Y	Surgery
21	2005	Chang ^[21]	72 M	L4-S1	Back pain, claudication	2 wk	Y	NA	NA	Y	Hypo	Hypo	Y	Surgery
22	2005	Chang ^[21]	66 F	L4-L5	Back pain, claudication	1 mo	Y	NA	NA	Y	Hypo	Hypo	Y	Surgery
23	2005	Chang ^[21]	63 M	L3-S1	Back pain, claudication, fever	2 wk	NA	NA	NA	N	Hypo	Hypo	Y	Surgery
24	2005	Kelly <i>et al</i> ^[22]	56 F	L4	Back pain, LE weakness	1 mo	Y	NA	RA, DM, RI	NA	Iso	Hypo	Y	L4-L5 lamina
25	2005	Mahmud <i>et al</i> ^[23]	47 M	L4-L5	Radiculopathy	3 mo	Y	NA	NA	Y	NA	NA	NA	L4-L5 lamina/facet
26	2005	Mahmud <i>et al</i> ^[23]	71 F	L4-L5	Back pain, radiculopathy	4 mo	N	NA	NA	N	NA	Hetero	NA	L4-L5 lamina/fusion
27	2005	Mahmud <i>et al</i> ^[23]	58 M	L4-L5	Back pain, claudication	6 mo	N	NA	NA	N	NA	Hyper	NA	L5 lamina
28	2005	Wazir <i>et al</i> ^[24]	66 F	C1-C2	Chronic neck pain, A-A subluxation, quadripareisis	2 mo	N	N	Arthritis	Y	NA	NA	NA	Lamina/fusion
29	2005	Yen <i>et al</i> ^[25]	65 F	L5-S1	Back pain, LE weakness	10 mo	N	NA	NA	NA	Iso	Hetero	Y	L5-S1 lamina
30	2006	Dharmadhikari <i>et al</i> ^[26]	66 F	C3-C7	Cord compression, quadripareisis, falls	2-3 mo	N	N	NA	NA	Hypo	Hypo	N	C3-C6 vertebrectomy
31	2006	Hou <i>et al</i> ^[27]	37 M	L5-S1	Back pain, fever	5 d	Y	N	RT	Y	Iso	Iso	Y	Medical NOS
32	2006	Oaks <i>et al</i> ^[28]	32 M	T5-T8	Back pain, myelopathy	NA	Y	NA	NA	NA	Hetero	Hetero	Y	Lamina
33	2006	Pankhania <i>et al</i> ^[29]	68 M	C4-C5	Neck pain, quadripareisis, sensory dysfunction	1 mo	N	N	NA	N	Iso	Hetero	Y	Lamina
34	2006	Popovich <i>et al</i> ^[30]	36 F	T2-T9	Paraplegia	2 wk	Y	NA	NA	Y	Hypo	Hypo	Y	T5-T7 lamina
35	2007	Adenwalla <i>et al</i> ^[31]	77 M	L5-S1	Severe low back pain, LE weakness	1 wk	N	N	Diuretic	Y	NA	NA	NA	Prednisone and colchicines
36	2007	Lam <i>et al</i> ^[32]	65 M	L3-L4	LE pain and numbness, BBD	Acute	Y	Y	RI	Y	NA	NA	NA	L3-L4 lamina
37	2007	Lam <i>et al</i> ^[32]	63 M	L4-S1	Chronic LE pain and paresthesia, claudication	1 yr	Y	N	NA	N	NA	NA	NA	L4-L5 lamina/fusion

38	2007	Suk <i>et al</i> ^[33]	55 M	L4-L5	Back pain, LE weakness and paresthesia, fever	1 wk	N	N	Alcohol	Y	Hypo	Hetero	Y	L4-L5 lamina/fusion
39	2008	Fontenet <i>et al</i> ^[34]	85 F	L3-L4	Low back pain	2 mo	N	N	Diuretics	Y	NA	Hyper	NA	Prednisone and colchicines
40	2009	Chan <i>et al</i> ^[35]	76 M	T8, T10	LE weakness		Y	Y	NA	Y	Iso	Hetero	NA	Medical NOS
41	2009	Nygaard <i>et al</i> ^[36]	75 M	L4-L5	Low back pain, fever	5 d	Y	N	NA	Y	NA	NA	NA	NA
42	2009	Tsai <i>et al</i> ^[37]	64 F	T8-T9	Fever, low back pain, LE weakness	1 d	N	N	DM, RI	N	Hypo	Iso	Y	T8-T9 discectomy and partial corpectomy
43	2010	Coulier <i>et al</i> ^[38]	62 F	C6-C7	Neck pain	NA	N	Y	NA	Y	NA	NA	NA	NA
44	2010	Ko <i>et al</i> ^[39]	63 M	L5-S1	Low back pain	2 mo	N	N	NA	Y	Hypo	Hypo	Y	Lamina
45	2010	Murphy <i>et al</i> ^[40]	82 M	NA	Back pain	3 mo	N	Y	NA	NA	NA	NA	NA	NA
46	2010	Ntsiba <i>et al</i> ^[41]	43 M	T9-T10	Spastic paraplegia	6 mo	Y	Y	Alcohol	NA	Hypo	Hyper	NA	T10 lamina
47	2010	Samuels <i>et al</i> ^[42]	75 M	L5-S1	Low back pain, radiculopathy, b/l groin pain	Acute	Y	N	DM, RI, arthritis	NA	NA	NA	NA	Steroid injection and allopurinol
48	2011	Ibrahim <i>et al</i> ^[43]	70 F	T1-T2	UE and LE weakness	1 yr	Y	N	RI	Y	Hypo	Hyper	NA	Lamina/fusion
49	2011	Levin <i>et al</i> ^[44]	34 M	T2-T5	Paraplegia	Acute	Y	N	RI, DM	Y	NA	NA	NA	Lamina
50	2011	Thavarajah <i>et al</i> ^[45]	57 M	C1-C2	Neck pain, UE and LE tingling	1 yr	Y	N	NA	NA	NA	NA	NA	C0-C6 fusion
51	2011	Tran <i>et al</i> ^[46]	73 M	C1-C2	CN IX, X, XII palsies, fever, cough,	3 d	Y	Y	RI	Y	NA	Hetero	NA	Allopurinol, rasburicase
52	2012	Federman <i>et al</i> ^[2]	66 M	C4-C6	Neck pain	4 mo	N	N	DM	Y	Hypo	Hetero	NA	Allopurinol, colchicine, narcotic analgesics
53	2012	Hasturk <i>et al</i> ^[4]	77 F	L4-L5	Low back pain, radiculopathy	5 mo	N	N	NA	N	Hypo	Hypo	Y	Surgery
54	2012	Sakamoto <i>et al</i> ^[3]	69 M	L1-L2	Back pain, radiculopathy	Acute	N	N	Heart Failure	Y	Hypo	Hypo	Y	Medical NOS
55	201	Yamamoto <i>et al</i> ^[47]	58 F	C4-C7	Malaise, fever, back pain	3 yr	N	Y	Arthritis, RI	Y	NA	NA	NA	Prednisolone, allopurinol, benzbromarone
56	2012	Lu <i>et al</i> ^[48]	29 M	L4-S1	Severe pain, paresthesia, acratia of LLE	3 yr	Y	Y	Chronic alcohol abuse, chronic gout	Y	Hypo	Hypo	NA	L4-L5/L5-S1 decompression/fusion
57	2012	Sanmillan <i>et al</i> ^[49]	71 M	C3-C4	Progressive Quadripareisis	4 mo	Y	Y	Hypertension, dislipidemia	Y	Hypo	Hyper	NA	C3-C4 micro-discectomy/fusion
58	2013	Wendling <i>et al</i> ^[50]	54 M	C5-C6	Inflammatory neck pain and cervicobrachial neuralgia	Acute	Y	N	Hypercholesterolemia	Y	Hypo	NA	Y	Colchicine
59	2013	Wendling <i>et al</i> ^[50]	52 F	Lumbar posterior facet joint	Low back pain	NA	N	Y	Polychondritis	N	NA	NA	NA	Surgery
60	2013	Wendling <i>et al</i> ^[50]	72 M	C5-C6	Acute neck pain, knee arthritis	Acute	Y	N	Hypertension	Y	NA	NA	NA	Colchicine
61	2013	Wendling <i>et al</i> ^[50]	65 M	L4-L5	Inflammatory low back pain	Acute	Y	Y	Cardiomyopathy, hypertension	Y	NA	NA	NA	Colchicine
62	2013	Wendling <i>et al</i> ^[50]	87 M	L3-L5	Inflammatory low back pain	Acute	N	Y	Hypertension, heart failure, chronic kidney failure	Y	Hypo	NA	Y	Colchicine
63	2013	Komarla <i>et al</i> ^[51]	69 F	L3-S1	Back pain, fever	Acute	N	Y	Alcohol abuse, chronic low back pain	N	NA	Hyper	NA	Allopurinol, colchicine, glucocorticoids
64	2013	de Parisot <i>et al</i> ^[52]	60 M	C1-C2	Walking disorders, urinary and bowel incontinence	6 mo	Y	Y	NA	Y	Hypo	Hyper	Y	C1-C2 Arthrodesis
65	2013	Kwan <i>et al</i> ^[53]	25 M	T9-T10, L3-S1	Pain, swelling, and decreased ROM in multiple joints	1 wk	N	Y	CKD	Y	Hypo	Hetero	NA	Prednisone, allopurinol

66	2013	Yoon <i>et al</i> ^[54]	64 M	T5-T7	Weakness B/L LE, back pain rad to left anterior chest, paraparesis	Weakness: Y (8 wk; back pain 1 mo ago)	Y	Acute gout arthritis 8 yr prior	Y	Hypo	Hetero	Y	T5-T7, laminectomy, facetectomy, pedicle screw fixation w/PL fusion	
67	2013	Jegapragasan <i>et al</i> ^[55]	24 M	L4-S1	Progressively worsening LBP w/rad, weakness of RLE, fever	3 yr LBP rad lat thigh	Y (4 yr Hx)	4 yr Tophaceous gout, CKD, 3 yr LBP, rad pain down later thigh (Rt > Lf)	Y	Iso	Hetero	NA	Decompressive laminectomy L4-S1, resection of intraspinal canal and perineural lesion; post-op: colchicine, allopurinol, brief burst of prednisone	
68	2014	Cardoso <i>et al</i> ^[56]	69 W	L4-5, SI joints	LBP rad to buttocks and hips, low fever	NA	N	Y	Constrictive pericarditis, chronic renal insufficiency, HTN, DM	Y	Hypo	Iso	Y	Colchicine, allopurinol

M: Male; F: Female; Sx: Symptoms; Hx: History; RT: Renal transplant; Hi: High; R: Right; LE: Lower extremity; RI: Renal insufficiency; BBD: Bowel/bladder dysfunction; Y and N: Yes and no; Hypo: Hypointense; Iso: Isointense; Hyper: Hyperintense; Hetero: Heterointense; UE: Upper extremity; Lamina: Laminectomy; Tx: Treatment; Gad: Gadolinium.

Table 2 Clinical features

No. of patients	
Localized back/neck pain	47
Spinal nerve root compression, in general	14
Radicular pain	6
Radiculopathy NOS	8
Spinal cord compression, in general	38
LE weakness	19
Quadriparesis	6
Claudication	5
Paraplegia	4
BBD	3
Myelopathy NOS	1
Cranial nerve palsy	1
Atlanto-axial subluxation	2
Fever	13

NOS: Not otherwise specified; UE: Upper extremity; LE: Lower extremity; BBD: Bowel/bladder dysfunction.

Table 3 Anatomic location of spinal gout

No. of patients	
Lumbar spine	38
Thoracic spine	15
Cervical spine	15
Not mentioned	1
Total ¹	68

¹Patient No. 65 had gout in two sites, thoracic and lumbar regions.

displayed bony erosion only, 5 (7.4%) demonstrated lytic lesions, and 2 (2.9%) were unremarkable.

Treatments

Forty-five (66.2%) patients had surgical treatment. Thirty-

Table 4 Laboratory studies

No. of patients	
Elevated uric acid	45
Elevated ESR	17
Elevated CRP	19
Renal insufficiency	11
Leukocytosis	9
Anemia	5

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

five (51.5%) patients had laminectomies, 8 (11.8%) of whom also had fusions with laminectomies, 7 (10.3%) had surgeries not otherwise specified, 1 (1.5%) had a vertebrectomy, 2 (2.9%) had discectomies with partial corpectomies. Twenty (29.4%) received medical treatment alone and 3 (4.4%) did not report any treatment (Table 6).

Case illustration

A 58-year-old female presented with a chief complaint of low back and radicular pain over left L4, 5 dermatomes that had been progressively worsening over a four-month duration to the point where she was unable to walk. The patient denied any saddle paresthesia or change in bowel and bladder function. She has a history of cardiovascular disease, chronic kidney disease (stage I), type II diabetes mellitus, hypertension, obesity, and obstructive sleep apnea. The patient also described an acute gouty arthropathy that was diagnosed in her right hand about 4 mo prior for which she was taking colchicine. An inflammatory workup was ordered which showed CRP of 3.58 (*n* < 1.0), ESR 25 (0-20), WBC 6.2 (4.0-10.0), uric acid 11.4 (2.5-6.8); HLA-B27, anti-DNA, Rheumatoid factor, and complement labs were negative.

Plain radiograph of the lumbar spine was unremark-

Table 5 Imaging studies	
No. of patients	
X-ray	
Not performed	37
Spondylosis/-listhesis	12
Bony erosion	8
Unremarkable	6
Degenerative changes	5
CT	
Not performed	35
BE and HDA	13
BE only	13
Lytic lesions	5
Unremarkable	2
MRI	
T1	
Not reported	28
Hypointense	31
Isointense	8
Heterointense	1
T2	
Not reported	24
Hypointense	18
Heterointense	12
Hyperintense	11
Isointense	4
Gadolinium enhancement	
No	36
Yes	32

BE: Bony erosion; HAD: High density attenuation; CT: Computed tomography; MRI: Magnetic resonance imaging.

Table 6 Treatment	
No. of patients	
Laminectomy only	24
Nonsurgical treatment	20
Surgery not specified	7
Laminectomy and fusion	5
Not reported	3
Fusion only	2
Laminectomy and facetectomy	3
Laminectomy and facetectomy and fusion	1
Vertebrectomy	1
Discectomy and partial corpectomy	2
Total	68

able. Plain radiograph of the right hand showed osseous erosive changes at the 4th finger distal interphalangeal (DIP) joint (Figure 1). MRI showed intraspinal extradural lesion causing spinal canal stenosis at L4-S1 (Figure 2). A CT showed that the lesion was calcified with erosive changes noted at the left L4-5 facet joint and L4 lamina (Figure 3). The patient was treated with L4-S1 decompression, instrumentation and fusion. The surgical microscope was used during excision of the intraspinal lesion, which appeared chalky white, non-adherent and easily peeled off the thecal sac without sustaining dural tear (Figure 4). Postoperatively the patient noted significant improvement in both low back and radicular pain. The patient received allopurinol treatment for gout



Figure 1 Plain radiograph anteroposterior view right hand showed osseous erosive changes at the 4th finger distal interphalangeal joint (arrow).

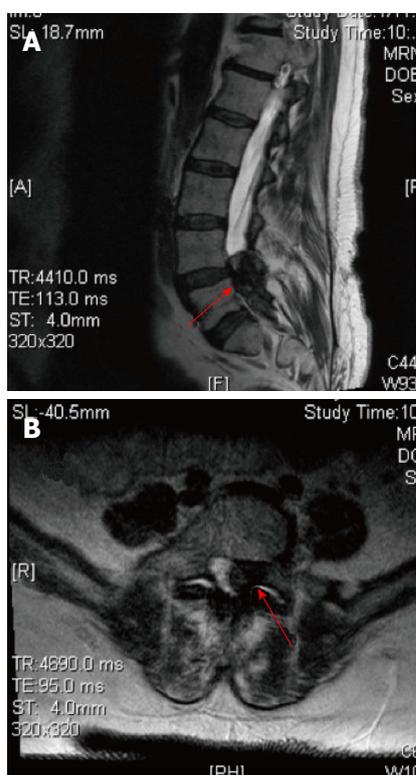


Figure 2 T2 weighted magnetic resonance imaging scan mid sagittal (A) and axial (B) showed intraspinal extradural hypodense lesion causing spinal canal stenosis at L4-S1.

and remained asymptomatic at the last follow up two years after the index procedure.

DISCUSSION

Gout is a common form of inflammatory arthritis caused by the deposition of MSU crystals in synovial joints that result into erosion and joint damage. Soft tissue masses of MSU crystals known as tophi are usually found in the hand and extensor surface of the forearm^[4,32,57]. Tophi are seen in patients with long-standing gout, but can also be one of the first symptoms amongst a cluster of metabolic disorders leading to hyperuricemia, especially

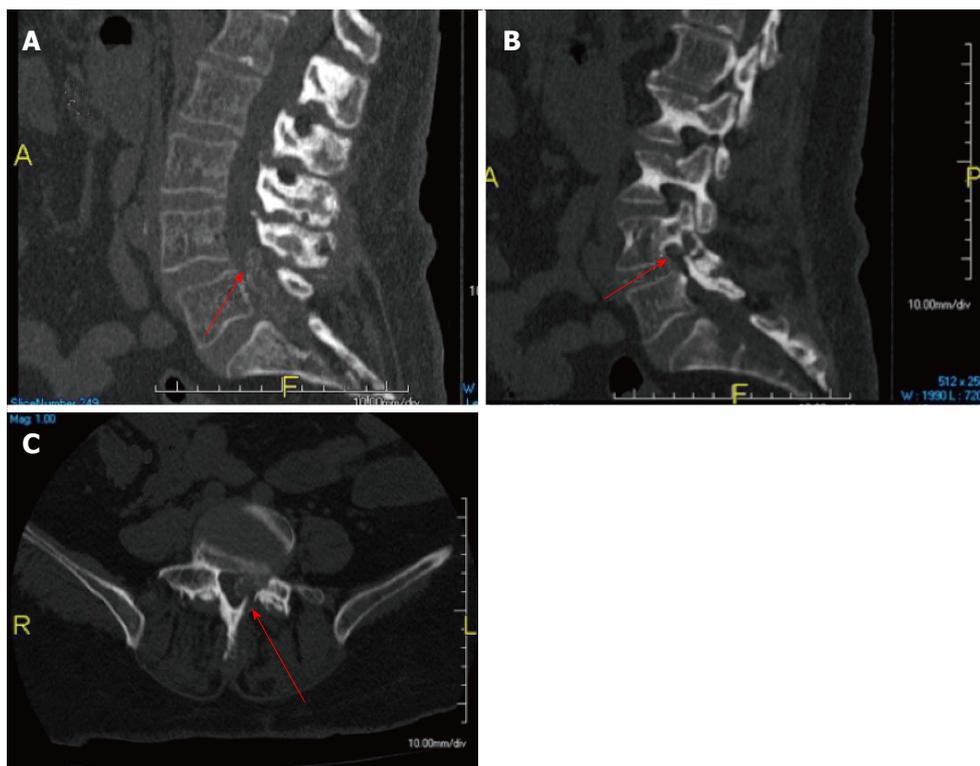


Figure 3 Computed tomography scan mid sagittal (A), left parasagittal (B), and axial (C) views showed the intraspinal lesion was calcified with erosive changes at the left L4-5 facet joint and L4 lamina (arrows).

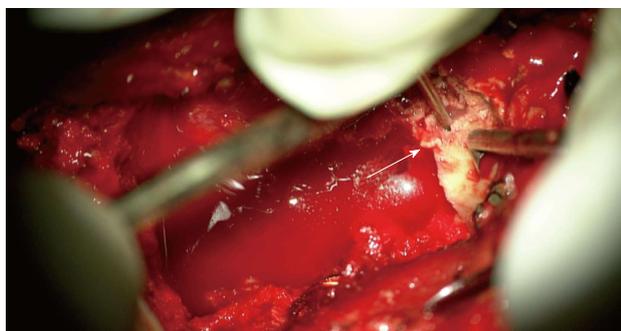


Figure 4 Intraoperative photograph taken by the surgical microscope showed a well-demarcated chalky white tophous lesion (arrow).

among those with long-standing renal impairment^[2,33]. Tophi are a common manifestation of gout, but spinal manifestations are considered rare. Recent research by de Mello *et al*^[1], however, suggests that tophi in the axial skeleton may be more prevalent than first suspected.

Although no studies have been able to conclude the exact mechanism for axial involvement in gout, the likely theory is, as gout usually involves joint spaces, facet joint may be the initial deposition location for MSU crystals. Another theory is based on the fact that high uric acid and other inflammatory markers are often elevated in gout. This increase in uric acid in the blood could signal a corresponding increase in cerebrospinal fluid (CSF) leading to the obstruction of the canal or foramen.

Literature review showed that the lumbar spine

was the most commonly involved region followed by thoracic and cervical regions. The most common clinical presentation was back pain associated with lumbar radiculopathy, or neurogenic claudication. The most frequent laboratory finding was hyperuricemia defined as uric acid above 7 mg/dL. Renal insufficiency was also found in many patients. Plain radiograph findings are usually non-specific. The most consistent image findings of the intraspinal extradural tophi were hypointense signal on the T1-weighted MRI and heterointense signals on the T2-weighted MRI. Spinal gout is usually diagnosed with cytological or histopathological studies. However, for patients treated with surgery, a pasty chalk-white mass are usually present. Clinical presentations and radiological findings of spinal gout are often non-specific and one has to consider the differential diagnoses of intraspinal extradural mass. The most frequent etiology with similar clinical presentations and imaging findings is herniated disc. Other causes include synovial cyst, tumor, epidural abscess, arteriovenous malformation.

Pharmacotherapy for spinal gout is the same as those used for gout involving typical joints. Acute gouty attack is most often treated with nonsteroidal anti-inflammatory drugs (NSAIDs), such as, naproxen or indomethacin. In patients with chronic kidney disease, duodenal or gastric ulcer, heart disease or hypertension, NSAID allergy, or anticoagulant treatment, colchicine is an alternative treatment. While NSAIDs and colchicine are effective in symptomatic reduction during an acute attack, they do not prevent the development of bony

erosions or tophi deposits in tissues. To prevent further gouty attack, maintenance medications are often prescribed with the goal of keeping uric acid level less than 6 mg/dL. Xanthine oxidase inhibitors, such as allopurinol, febuxostat, and oxypurinol, are the first line choices for reduced production of uric acid. Allopurinol can precipitate gouty attack or worsen current attack, thus, it is used for maintenance after acute attack has resolved. Uricosuric agents, such as, probenecid and sulfapyrazone, are second line prophylactics aimed to increase uric acid excretion since decreased uric acid excretion is responsible for 85% to 90% of primary or secondary hyperuricemia^[58].

Surgical interventions may be needed if patient has symptoms of spinal cord or nerve root compression. The mainstay of surgical treatment is decompression and excision of the tophi. The role of fusion at the time of the decompression remains controversial. The need for fusion is influenced by symptomatic preoperative instability as evidenced by dynamic radiographs, erosion of the facet joint seen on CT scan, or intraoperative instability that may be created by iatrogenic resection of spinal structures such as the pars interarticularis or the facet joints.

Although this article provides a broad overview of cases involving spinal gout since January 2000, there are some limitations. The absence of certain information, such as the post-treatment outcomes, limited the depth of our analysis in certain cases. Furthermore, the literature review could not always account for individual variation among the 68 cases reviewed including the particular method of diagnosis, which was not standardized across all patients included in the study. In addition, the individual articles did not provide information regarding prior uric acid lowering treatments, which could possibly inflate the number of spinal gout cases with normal uric acid levels.

The majority of clinical features for spinal gout such as back pain and neurological symptoms are nonspecific. Thus, one must rule out other common diagnoses, such as disc herniation, tumor, infection prior to diagnosing a patient with spinal gout. Laboratory study indicative of gout is elevated uric acid levels. In this literature review, the majority of the cases utilized MRI as the radiological study of choice in detecting spinal gout. While MRI was the major non-invasive diagnostic method, all suspicious findings on imaging required surgical sampling for pathological confirmation of negatively birefringent MSU crystals presence.

COMMENTS

Background

Gout is a common inflammatory arthritis with an increase in prevalence over the last 20 years. It currently affects over 8 million Americans. The primary aim of this review is to summarize the most common presenting features, imaging findings, and treatment choices based on the 68 published cases.

Research frontiers

Literature review showed that the lumbar spine was the most commonly

involved region followed by thoracic and cervical regions. The most common clinical presentation was back pain associated with lumbar radiculopathy, or neurogenic claudication. The most frequent laboratory finding was hyperuricemia defined as uric acid above 7 mg/dL.

Innovations and breakthroughs

Traditionally gout thought of as a rare problem characterized by a sudden, severe attacks of pain, redness and tenderness in joints, often the joint at the base of the big toe. Recent studies suggest that axial gout may be more prevalent than suspected. Spinal gout can affect the facet joint, laminae, ligamentum flavum, as well as the epidural spaces.

Applications

The majority of clinical features for spinal gout such as back pain and neurological symptoms are nonspecific. Suspicious findings on MRI imaging required surgical sampling for pathological confirmation of negatively birefringent monosodium urate crystals presence.

Peer-review

It is a good review concerning the spinal gout consisting of the symptom and signs, treatment option and lab data analysis.

REFERENCES

- 1 **de Mello FM**, Helito PV, Bordalo-Rodrigues M, Fuller R, Halpern AS. Axial gout is frequently associated with the presence of current tophi, although not with spinal symptoms. *Spine (Phila Pa 1976)* 2014; **39**: E1531-E1536 [PMID: 25271500 DOI: 10.1097/BRS.0000000000000633]
- 2 **Federman DG**, Kravetz JD, Luciano RL, Brown JE. Gout: what a pain in the neck. *Conn Med* 2012; **76**: 143-146 [PMID: 22666972]
- 3 **Sakamoto FA**, Winalski CS, Rodrigues LC, Fernandes AR, Bortoletto A, Sundaram M. Radiologic case study. *Orthopedics* 2012; **35**: 353-437 [PMID: 22588390 DOI: 10.3928/01477447-20120426-01]
- 4 **Hasturk AE**, Basmaci M, Canbay S, Vural C, Erten F. Spinal gout tophus: a very rare cause of radiculopathy. *Eur Spine J* 2012; **21** Suppl 4: S400-S403 [PMID: 21594750]
- 5 **Kao MC**, Huang SC, Chiu CT, Yao YT. Thoracic cord compression due to gout: a case report and literature review. *J Formos Med Assoc* 2000; **99**: 572-575 [PMID: 10925570]
- 6 **Mekelburg K**, Rahimi AR. Gouty arthritis of the spine: clinical presentation and effective treatments. *Geriatrics* 2000; **55**: 71-74 [PMID: 10771704]
- 7 **Paquette S**, Lach B, Guiot B. Lumbar radiculopathy secondary to gouty tophi in the filum terminale in a patient without systemic gout: case report. *Neurosurgery* 2000; **46**: 986-988 [PMID: 10764275 DOI: 10.1097/00006123-200004000-00042]
- 8 **Thornton FJ**, Torreggiani WC, Brennan P. Tophaceous gout of the lumbar spine in a renal transplant patient: a case report and literature review. *Eur J Radiol* 2000; **36**: 123-125 [PMID: 11091009 DOI: 10.1016/S0720-048X(00)00214-X]
- 9 **Barrett K**, Miller ML, Wilson JT. Tophaceous gout of the spine mimicking epidural infection: case report and review of the literature. *Neurosurgery* 2001; **48**: 1170-1172 [PMID: 11334288 DOI: 10.1097/00006123-200105000-00046]
- 10 **St George E**, Hillier CE, Hatfield R. Spinal cord compression: an unusual neurological complication of gout. *Rheumatology (Oxford)* 2001; **40**: 711-712 [PMID: 11426037 DOI: 10.1093/rheumatology/40.6.711]
- 11 **Wang LC**, Hung YC, Lee EJ, Chen HH. Acute paraplegia in a patient with spinal tophi: a case report. *J Formos Med Assoc* 2001; **100**: 205-208 [PMID: 11393117]
- 12 **Hsu CY**, Shih TT, Huang KM, Chen PQ, Sheu JJ, Li YW. Tophaceous gout of the spine: MR imaging features. *Clin Radiol* 2002; **57**: 919-925 [PMID: 12413917 DOI: 10.1053/crad.2001.1001]
- 13 **Souza AW**, Fontenele S, Carrete H, Fernandes AR, Ferrari AJ. Involvement of the thoracic spine in tophaceous gout. A case

- report. *Clin Exp Rheumatol* 2002; **20**: 228-230 [PMID: 12051405]
- 14 **Yen HL**, Cheng CH, Lin JW. Cervical myelopathy due to gouty tophi in the intervertebral disc space. *Acta Neurochir (Wien)* 2002; **144**: 205-207 [PMID: 11862523 DOI: 10.1007/s007010200026]
 - 15 **Diaz A**, Porhiel V, Sabatier P, Taha S, Ragragui O, Comoy J, Leriche B. [Tophaceous gout of the cervical spine, causing cord compression. Case report and review of the literature]. *Neurochirurgie* 2003; **49**: 600-604 [PMID: 14735005]
 - 16 **Draganescu M**, Leventhal LJ. Spinal gout: case report and review of the literature. *J Clin Rheumatol* 2004; **10**: 74-79 [PMID: 17043470 DOI: 10.1097/01.rhu.0000120898.82192.f4]
 - 17 **El Sandid M**, Ta H. Another presentation of gout. *Ann Intern Med* 2004; **140**: W32 [PMID: 15096364 DOI: 10.7326/0003-4819-140-8-200404200-00037-w2]
 - 18 **Nakajima A**, Kato Y, Yamanaka H, Ito T, Kamatani N. Spinal tophaceous gout mimicking a spinal tumor. *J Rheumatol* 2004; **31**: 1459-1460 [PMID: 15229971]
 - 19 **Beier CP**, Hartmann A, Woertgen C, Brawanski A, Rothoerl RD. A large, erosive intraspinal and paravertebral gout tophus. Case report. *J Neurosurg Spine* 2005; **3**: 485-487 [PMID: 16381213 DOI: 10.3171/spi.2005.3.6.0485]
 - 20 **Celik SE**, Görgülü M. Tophaceous gout of the atlantoaxial joint. Case illustration. *J Neurosurg Spine* 2005; **2**: 230 [PMID: 15739541 DOI: 10.3171/spi.2005.2.2.0230]
 - 21 **Chang IC**. Surgical versus pharmacologic treatment of intraspinal gout. *Clin Orthop Relat Res* 2005; **(433)**: 106-110 [PMID: 15805944 DOI: 10.1097/01.blo.0000151456.52270.39]
 - 22 **Kelly J**, Lim C, Kamel M, Keohane C, O'Sullivan M. Topacheous gout as a rare cause of spinal stenosis in the lumbar region. Case report. *J Neurosurg Spine* 2005; **2**: 215-217 [PMID: 15739537 DOI: 10.3171/spi.2005.2.2.0215]
 - 23 **Mahmud T**, Basu D, Dyson PH. Crystal arthropathy of the lumbar spine: a series of six cases and a review of the literature. *J Bone Joint Surg Br* 2005; **87**: 513-517 [PMID: 15795202 DOI: 10.1302/0301-620X.87B4.15555]
 - 24 **Wazir NN**, Moorthy V, Amalourde A, Lim HH. Tophaceous gout causing atlanto-axial subluxation mimicking rheumatoid arthritis: a case report. *J Orthop Surg (Hong Kong)* 2005; **13**: 203-206 [PMID: 16131689]
 - 25 **Yen PS**, Lin JF, Chen SY, Lin SZ. Tophaceous gout of the lumbar spine mimicking infectious spondylodiscitis and epidural abscess: MR imaging findings. *J Clin Neurosci* 2005; **12**: 44-46 [PMID: 15639411]
 - 26 **Dharmadhikari R**, Dildey P, Hide IG. A rare cause of spinal cord compression: imaging appearances of gout of the cervical spine. *Skeletal Radiol* 2006; **35**: 942-945 [PMID: 16547746 DOI: 10.1007/s00256-006-0088-2]
 - 27 **Hou LC**, Hsu AR, Veeravagu A, Boakye M. Spinal gout in a renal transplant patient: a case report and literature review. *Surg Neurol* 2007; **67**: 65-73; discussion 73 [PMID: 17210304 DOI: 10.1016/j.surneu.2006.03.038]
 - 28 **Oaks J**, Quarfordt SD, Metcalfe JK. MR features of vertebral tophaceous gout. *AJR Am J Roentgenol* 2006; **187**: W658-W659 [PMID: 17114521 DOI: 10.2214/AJR.06.0661]
 - 29 **Pankhania AC**, Patankar T, Du Plessis D. Neck pain: an unusual presentation of a common disease. *Br J Radiol* 2006; **79**: 537-539 [PMID: 16714761 DOI: 10.1259/bjr/28763793]
 - 30 **Popovich T**, Carpenter JS, Rai AT, Carson LV, Williams HJ, Marano GD. Spinal cord compression by tophaceous gout with fluorodeoxyglucose-positron-emission tomographic/MR fusion imaging. *AJNR Am J Neuroradiol* 2006; **27**: 1201-1203 [PMID: 16775264]
 - 31 **Adenwalla HN**, Usman MH, Baqir M, Zulqarnain M, Shah H. Vertebral gout and ambulatory dysfunction. *South Med J* 2007; **100**: 413-414 [PMID: 17458408 DOI: 10.1097/SMJ.0b013e3180374de1]
 - 32 **Lam HY**, Cheung KY, Law SW, Fung KY. Crystal arthropathy of the lumbar spine: a report of 4 cases. *J Orthop Surg (Hong Kong)* 2007; **15**: 94-101 [PMID: 17429128]
 - 33 **Suk KS**, Kim KT, Lee SH, Park SW, Park YK. Tophaceous gout of the lumbar spine mimicking pyogenic discitis. *Spine J* 2007; **7**: 94-99 [PMID: 17197341 DOI: 10.1016/j.spinee.2006.01.009]
 - 34 **Fontenot A**, Harris P, Macasa A, Menon Y, Quinet R. An initial presentation of polyarticular gout with spinal involvement. *J Clin Rheumatol* 2008; **14**: 188-189 [PMID: 18525444 DOI: 10.1097/RHU.0b013e318177a6b2]
 - 35 **Chan AT**, Leung JL, Sy AN, Wong WW, Lau KY, Ngai WT, Tang VW. Thoracic spinal gout mimicking metastasis. *Hong Kong Med J* 2009; **15**: 143-145 [PMID: 19342742]
 - 36 **Nygaard HB**, Shenoi S, Shukla S. Lower back pain caused by tophaceous gout of the spine. *Neurology* 2009; **73**: 404 [PMID: 19652147 DOI: 10.1212/WNL.0b013e3181b04cb1]
 - 37 **Tsai CH**, Chen YJ, Hsu HC, Chen HT. Bacteremia coexisting with tophaceous gout of the spine mimicking spondylodiscitis: a case report. *Spine (Phila Pa 1976)* 2009; **34**: E106-E109 [PMID: 19139655 DOI: 10.1097/BRS.0b013e31818d051a]
 - 38 **Coulier B**, Tancredi MH. Articular tophaceous gout of the cervical spine: CT diagnosis. *JBR-BTR* 2010; **93**: 325 [PMID: 21381540]
 - 39 **Ko KH**, Huang GS, Chang WC. Tophaceous gout of the lumbar spine. *J Clin Rheumatol* 2010; **16**: 200 [PMID: 20511985 DOI: 10.1097/RHU.0b013e3181c51ea9]
 - 40 **Murphy DJ**, Shearman AL, Mascarenhas R, Haigh RC. Lucent lesions of the spine--a case of spinal gout. *Age Ageing* 2010; **39**: 660 [PMID: 20551168 DOI: 10.1093/ageing/afq070]
 - 41 **Ntsiba H**, Makosso E, Moyikoua A. Thoracic spinal cord compression by a tophus. *Joint Bone Spine* 2010; **77**: 187-188 [PMID: 20153678]
 - 42 **Samuels J**, Keenan RT, Yu R, Pillinger MH, Bescke T. Erosive spinal tophus in a patient with gout and back pain. *Bull NYU Hosp Jt Dis* 2010; **68**: 147-148 [PMID: 20632992]
 - 43 **Ibrahim GM**, Ebinu JO, Rubin LA, de Tilly LN, Spears J. Gouty arthropathy of the axial skeleton causing cord compression and myelopathy. *Can J Neurol Sci* 2011; **38**: 918-920 [PMID: 22030432]
 - 44 **Levin E**, Hurth K, Joshi R, Brasington R. Acute presentation of tophaceous myelopathy. *J Rheumatol* 2011; **38**: 1525-1526 [PMID: 21724731 DOI: 10.3899/jrheum.101335]
 - 45 **Thavarajah D**, Hussain R, Martin JL. Cervical arthropathy caused by gout: stabilisation without decompression. *Eur Spine J* 2011; **20** Suppl 2: S231-S234 [PMID: 20938786]
 - 46 **Tran A**, Prentice D, Chan M. Tophaceous gout of the odontoid process causing glossopharyngeal, vagus, and hypoglossal nerve palsies. *Int J Rheum Dis* 2011; **14**: 105-108 [PMID: 21303490 DOI: 10.1111/j.1756-185X.2010.01565.x]
 - 47 **Yamamoto M**, Tabeya T, Masaki Y, Suzuki C, Naishiro Y, Ishigami K, Yajima H, Shimizu Y, Obara M, Yamamoto H, Sugaya T, Takahashi H, Imai K, Shinomura Y. Tophaceous gout in the cervical spine. *Intern Med* 2012; **51**: 325-328 [PMID: 22293812 DOI: 10.2169/internalmedicine.51.6262]
 - 48 **Lu F**, Jiang J, Zhang F, Xia X, Wang L, Ma X. Lumbar spinal stenosis induced by rare chronic tophaceous gout in a 29-year-old man. *Orthopedics* 2012; **35**: e1571-e1575 [PMID: 23027501]
 - 49 **Sanmillan Blasco JL**, Vidal Sarro N, Marnov A, Acebes Martín JJ. Cervical cord compression due to intradiscal gouty tophus: brief report. *Spine (Phila Pa 1976)* 2012; **37**: E1534-E1536 [PMID: 22914704 DOI: 10.1097/BRS.0b013e31826f2886]
 - 50 **Wendling D**, Prati C, Hoen B, Godard J, Vidon C, Godfrin-Valnet M, Guillot X. When gout involves the spine: five patients including two inaugural cases. *Joint Bone Spine* 2013; **80**: 656-659 [PMID: 23835305]
 - 51 **Komarla A**, Schumacher R, Merkel PA. Spinal gout presenting as acute low back pain. *Arthritis Rheum* 2013; **65**: 2660 [PMID: 23818092]
 - 52 **de Parisot A**, Ltaief-Boudrigua A, Villani AP, Barrey C, Chapurlat RD, Confavreux CB. Spontaneous odontoid fracture on a tophus responsible for spinal cord compression: a case report. *Joint Bone Spine* 2013; **80**: 550-551 [PMID: 23566667]
 - 53 **Kwan BY**, Osman S, Barra L. Spinal gout in a young patient with involvement of thoracic, lumbar and sacroiliac regions. *Joint Bone Spine* 2013; **80**: 667-668 [PMID: 23566660]
 - 54 **Yoon JW**, Park KB, Park H, Kang DH, Lee CH, Hwang SH, Jung

- JM, Han JW, Park IS. Tophaceous gout of the spine causing neural compression. *Korean J Spine* 2013; **10**: 185-188 [PMID: 24757485 DOI: 10.14245/kjs.2013.10.3.185]
- 55 **Jegapragasan M**, Calniquer A, Hwang WD, Nguyen QT, Child Z. A case of tophaceous gout in the lumbar spine: a review of the literature and treatment recommendations. *Evid Based Spine Care J* 2014; **5**: 52-56 [PMID: 24715872 DOI: 10.1055/s-0034-1366979]
- 56 **Cardoso FN**, Omoumi P, Wieers G, Maldague B, Malghem J, Lecouvet FE, Vande Berg BC. Spinal and sacroiliac gouty arthritis: report of a case and review of the literature. *Acta Radiol Short Rep* 2014; **3**: 2047981614549269 [PMID: 25346852 DOI: 10.1177/2047981614549269]
- 57 **Hasegawa EM**, de Mello FM, Goldenstein-Schainberg C, Fuller R. Gout in the spine. *Rev Bras Reumatol* 2013; **53**: 296-302 [PMID: 24051913 DOI: 10.1590/S0482-50042013000300008]
- 58 **Bull PW**, Scott JT. Intermittent control of hyperuricemia in the treatment of gout. *J Rheumatol* 1989; **16**: 1246-1248 [PMID: 2681764]

P- Reviewer: Hammoudeh M, Pan HC **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>



World Journal of *Orthopedics*

World J Orthop 2016 December 18; 7(12): 776-846



Editorial Board

2015-2018

The *World Journal of Orthopedics* Editorial Board consists of 329 members, representing a team of worldwide experts in orthopedics. They are from 41 countries, including Australia (10), Austria (8), Bangladesh (1), Belgium (4), Brazil (10), Canada (4), Chile (1), China (29), Croatia (2), Cyprus (1), Denmark (2), Egypt (5), Finland (1), France (2), Germany (19), Greece (12), Hungary (1), India (17), Iran (4), Israel (6), Italy (21), Japan (14), Jordan (2), Malaysia (1), Netherlands (10), New Zealand (1), Poland (1), Saudi Arabia (2), Serbia (1), Singapore (4), Slovenia (2), South Korea (12), Spain (7), Sri Lanka (1), Sweden (8), Switzerland (4), Thailand (5), Turkey (11), United Arab Emirates (1), United Kingdom (17), and United States (65).

EDITORS-IN-CHIEF

Quanjun (Trey) Cui, *Charlottesville*
Bao-Gan Peng, *Beijing*

ASSOCIATE EDITOR

Wasim S Khan, *London*

GUEST EDITORIAL BOARD MEMBERS

Yuk-Kwan Chen, *Kaohsiung*
Sheng-Mou Hou, *Taipei*
Tsan-Wen Huang, *Pu-Tz City*
Yen-Hsuan Jean, *Pingtung*
Ko-Hsiu Lu, *Tai chung*
Wei-Ren Su, *Tainan*
Yih-Wen Tarn, *Kaohsiung*
Kuo-Wei Wang, *Kaohsiung*
James Cheng-Chung Wei, *Tai chung*

MEMBERS OF THE EDITORIAL BOARD



Australia

Nicky Bertollo, *Sydney*
Stuart Adam Callary, *Adelaide*
Changhai Ding, *Hobart*
Herwig Drobotz, *Mackay*
Melanie Jane Franklyn, *Melbourne*
Laurent Frossard, *Brisbane*
Pazit Levinger, *Melbourne*
Munjed Al Muderis, *Sydney*
Gordon L Slater, *Sydney*
Lucian Bogdan Solomon, *Adelaide*



Austria

Christian Krasny, *Vienna*
Florian M Kovar, *Vienna*
Gerold Labek, *Innsbruck*

Stefan Marlovits, *Vienna*
Lukas Leopold Negrin, *Himberg*
Reinhold Ortmaier, *Salzburg*
Patrick Sadoghi, *Graz*
Klemens Trieb, *Wels*



Bangladesh

Saidur Rahman Mashreky, *Dhaka*



Belgium

Olivier Bruyere, *Liege*
Andre Farasyn, *Ghent*
Tom Van Leemput, *Zandhoven*
Geert Meermans, *Berchem*



Brazil

Rogério Serpone Bueno, *Sao Paulo*
Gustavo Constantino de Campos, *Campinas*
Reginaldo K Fukuchi, *Sao Paulo*
Tiago Lazzaretti Fernandes, *Sao Paulo*
Mauro Cesar de Moraes Filho, *Sao Paulo*
Alexandre Leme Godoy-Santos, *Sao Paulo*
Andrei Fernandes Joaquim, *Campinas*
Daniel F Martins, *Palhoca*
Leonardo Metsavaht, *Rio de Janeiro*
Francis Trombini-Souza, *Sao Paulo*



Canada

Kivanc Atesok, *Etobicoke*
Marwan El-Rich, *Edmonton*
Richard Kremer, *Montreal*
Neetu Rishiraj, *Vancouver*



Chile

Dante Parodi, *Santiago*



China

Wing-Hoi Cheung, *Hong Kong*
Lin Guo, *Chongqing*
Yong Qiang Hao, *Shanghai*
Chen Jiao, *Beijing*
Winson Chiu-Chun Lee, *Hong Kong*
Jian-Min Li, *Jinan*
Pauline Po Yee Lui, *Hong Kong*
Dong-Yang Ma, *Lanzhou*
Wei-Min Pan, *Xi'an*
Bao-Gan Peng, *Beijing*
Kang-Lai Tang, *Chongqing*
Defeng Wang, *Hong Kong*
Yu Wang, *Beijing*
Qing Xia, *Shanghai*
Ya-Yi Xia, *Lanzhou*
Xi-Jie Yu, *Chengdu*
Xiao-Lei Zhang, *Wenzhou*
Jian-Hua Zhao, *Chongqing*
Jian-Ning Zhao, *Nanjing*
Ping Zhen, *Lanzhou*



Croatia

Goran Bicanic, *Zagreb*
Srecko Sabalic, *Zagreb*



Cyprus

Michalis Zenios, *Limassol*



Denmark

Lars C Borris, *Arhus*
Morten Tange Kristensen, *Hvidovre*



Egypt

Barakat Sayed El-Alfy, *Mansoura*
Khaled M Emara, *Cairo*
Mohamed Mostafa Hosney El-Sayed, *Tanta*
Mohammad Masoud, *Assiut*
Elsayed Ibraheem Elsayed Massoud, *Sohag*



Finland

Hannu T Aro, *Turku*



France

Federico Canavese, *Clermont Ferrand*
Hechmi Toumi, *Orleans*



Germany

Ahmet Ali Altintas, *Koln*
Hagen Andruszkow, *Aachen*
Mike H Baums, *Wiesbaden*
Peter Bernstein, *Dresden*
Bilal Farouk El-Zayat, *Marburg*
Ahmad M Eweida, *Ludwigshafen*
Chrisitan B Frank, *Baden-Baden*
Michael Frink, *Marburg*
Andreas B Imhoff, *Munich*
Chlodwig Kirchhoff, *Munich*
Matthias Knoke, *Aachen*
Hans-Christoph Pape, *Aachen*
Markus Peter Regauer, *Munich*
Khaled Hamed Salem, *Paderborn*
Frank M Schiedel, *Muenster*
Volker Schoeffl, *Bamberg*
Hagen Schmal, *Freiburg*
Fritz Thorey, *Heidelberg*
Tobias Topp, *Berlin*



Greece

Antonios Angoules, *Athens*
Georgios I Drosos, *Alexandroupolis*
Konstantinos Fousekis, *Egio*
Michael Hantes, *Larissa*
Marios G Lykissas, *Athens*
George A Macheras, *Athens*
Konstantinos N Malizos, *Larissa*
Dimitrios Nikolopoulos, *Athens*
Vassilis Paschalis, *Trikala*
Dionysios J Papachristou, *Patras*
Georgios Constantinos Papachristou, *Athens*
Haris S Vasiliadis, *Ioannina*



Hungary

Andor Sebestyén, *Pécs*



India

Vikas Bachhal, *Chandigarh*
Roopesh Kumar VR, *Pondicherry*
Vikas Kulshrestha, *Delhi*
Ashokkumar Navratnamal Johari, *Mumbai*
Prمود V Lokhande, *Pune*
Vivek Mahajan, *New Delhi*
Karthik Selvaraj Murugappan, *Coimbatore*
Satya Ranjan Patra, *Bhubaneswar*
V Prakash, *Anand*
Joshua Samuel Rajkumar, *MPT, Bangalore*
Parag Sancheti, *Pune*
Gaurav Sharma, *Chandigarh*
Mohamed Shafi, *Gangavalli*
Ajay Pal Singh, *Punjab*
Sujit Kumar Tripathy, *Bhubaneswar*
Raju Vaishya, *New Delhi*
Divya Vohora, *New Delhi*



Iran

MT Karimi, *Isfahan*
Firooz Madadi, *Tehran*
Mohammad Ali Mohseni-Bandpei, *Tehran*
Amir Hossein Saveh, *Tehran*



Israel

Alexander Blankstein, *Ramat HaSharon*
Itay Fenichel, *Udim*
Youssef Maher Masharawi, *Tel Aviv*
Nahum Rosenberg, *Haifa*
Jona J Sela, *Jerusalem*
Yehuda Ullmann, *Haifa*



Italy

Alessandro Aprato, *Torino*
Andrea Angelini, *Bologna*
Luigi Valentino Berra, *Milano*
Matteo Cadossi, *Bologna*
Lawrence Camarda, *Palermo*
Giuseppe Maurizio Campo, *Messina*
Andrea Camera, *Pietra Ligure*
Stefano Carbone, *Rome*
Patrizia D'Amelio, *Torino*
Cesare Faldini, *Bologna*
Olimpio Galasso, *Catanzaro*
Umile Giuseppe Longo, *Roma*
Alberto Grassi, *Bologna*
Nicolò Martinelli, *Milan*
Raffaele Mugnai, *Modena*
Giuseppe Musumeci, *Catania*
Roberto Postacchini, *Rome*
Barbara Rossi, *Rome*
Roberto Rossi, *Torino*

Stefano Marco Paolo Rossi, *Pavia*
Luigi Tarallo, *Modena*



Japan

Ukei Anazawa, *Ichikawa*
Yoichi Aota, *Yokohama*
Masahiro Hasegawa, *Tsu City*
Takafumi Hiranaka, *Takatsuki*
Eichi Itadera, *Narita*
Hiroshi Kawaguchi, *Tokyo*
Shigeru Kobayashi, *Eiheiji*
Makoto Makishima, *Itabashi-ku*
Kanji Mori, *Otsu*
Tsuyoshi Ohishi, *Hamamatsu*
Kazuya Oshima, *Osaka*
Hirotaka Sano, *Sendai*
Jun Takahashi, *Matsumoto*
Kotaro Yamakado, *Fukui*



Jordan

Alia A Alghwiri, *Amman*
Bashar Abuzayed, *Irbid*



Malaysia

Areezo Eshraghi, *Kuala Lumpur*



Netherlands

Michel Pieter Jozef van den Bekerom, *Amsterdam*
Peter RG Brink, *Maastricht*
Yvon Marielle den Hartog, *Rotterdam*
Izaak Frederik Kodde, *Amsterdam*
Jesse WP Kuiper, *Alkmaar*
Tom M van Raaij, *Groningen*
Hugo Christiaan van der Veen, *Groningen*
Alexander TM van de Water, *Enschede*
Walter van der Weegen, *Geldrop*
Eline W Zwitser, *Leiderdorp*



New Zealand

Gary J Hooper, *Christchurch*



Poland

Agnieszka Tomaszewska, *Gdańsk*



Saudi Arabia

Ahmed Bakhsh, *Al-Khobar*
Mohamed Zamzam, *Riyadh*



Serbia

Miroslav Ziva Milankov, *Novi Sad*



Singapore

Yee Han Dave Lee, *Singapore*
 Anselm Mak, *Singapore*
 Sean Ng, *Singapore*
 Ken Lee Puah, *Singapore*



Slovenia

Gregor Recnik, *Maribor*
 Matjaz Sajovic, *Celje*



South Korea

Yong Ahn, *Seoul*
 Seung-Hoon Baek, *Daegu*
 Chang-Ho Hwang, *Ulsan*
 Jin Ho Hwang, *Seoul*
 Jung-Taek Hwang, *Chuncheon*
 Tae-Young Kim, *Anyang*
 Sung-Uk Kuh, *Seoul*
 Haejung Lee, *Busan*
 Young-Kyun Lee, *Seongnam*
 Soon Hyuck Lee, *Seoul*
 Sang-Ki Lee, *Daejeon*
 Hee-Soo Seo, *Seoul*



Spain

Miguel Angel Ruiz Iban, *Madrid*
 Rafael Arriaza, *La Coruna*
 Enrique Guerado, *Malaga*
 Albert Isidro, *Barcelona*
 Sergio Hernandez-Sanchez, *Sant Joan D'alacant*
 Nuria Vilaboa, *Madrid*
 Rafael Villalba, *Córdoba*



Sri Lanka

Janaka Lenora, *Galle*



Sweden

Allan Abbott, *Linkoping*
 Paul W Ackermann, *Enebyberg*
 Johan von Heideken, *Stockholm*
 Karin Larsson, *Gothenburg*
 Anna Nordstrom, *Umea*
 Yan Li, *Stockholm*
 Jonas Ranstam, *Lund*
 Ola Rolfson, *Gothenburg*



Switzerland

Marco Barbero, *Manno*

Dimitrios-Stergios Evangelopoulos, *Bern*
 Ladislav Mica, *Zurich*
 Michael Tobias Hirschmann, *Bruderholz*



Thailand

Sugalya Amatachaya, *Maung*
 Theerachai Apivatthakakul, *Chiang Mai*
 Wiroon Laupattarakasem, *Mueang*
 Boonsin Tangtrakulwanich, *Hat Yai*
 Tulyapruet Tawonsawatruk, *Bangkok*



Turkey

Tuncay Colak, *Kocaeli*
 Abdullah Demirtas, *Istanbul*
 Mehmet Erdil, *Istanbul*
 Kemal Gokkus, *Antalya*
 Alper Kaya, *Istanbul*
 Serdar Kahraman, *Istanbul*
 Ramazan Kahveci, *Ankara*
 Yavuz Kocabey, *Kocaeli*
 sKemal Nas, *Sakarya*
 Salih Ozgocmen, *Kayseri*
 Namik Sahin, *Bursa*



United Arab Emirates

Ashraf Fathi Hefny, *Al Ain*



United Kingdom

Nawfal Al-Hadithy, *London*
 Sarah Cartmell, *Manchester*
 Nick Caplan, *Newcastle upon Tyne*
 Andrew Douglas Carrothers, *Cambridge*
 Efsthios Drampalos, *Wigan*
 Prithee Jettoo, *Middlesbrough*
 Saravana Vail Karuppiyah, *Nottingham*
 Hammad Malik, *Manchester*
 Riazuddin Mohammed, *Wigan*
 Gohar Naqvi, *Cambridge*
 Christopher William Oliver, *Edinburgh*
 Philip Socrates Pastides, *London*
 Greg A Robertson, *Edinburgh*
 Adnan Saithna, *Liverpool*
 Praveen Sarda, *Gillingham*
 Deepak Gubbi Shivarathre, *Liverpool*



United States

Daniel Louis Aaron, *Pawtucket*
 Ashish Anand, *Jackson*
 Huston Davis Adkisson, *St Louis*
 Keith Baldwin, *Philadelphia*

Adam Brufsky, *Pittsburgh*
 Ali Bydon, *Baltimore*
 Nicole J Chimera, *Amherst*
 Ock K Chun, *Storrs*
 Suresh Chinthakunta, *Collegeville*
 Alan H Daniels, *Providence*
 Nabanita S Datta, *Detroit*
 Deanna C Dye, *Bozeman*
 Scott Forsyth Dye, *San Francisco*
 Clark Dickin, *Muncie*
 Hossein Elgafy, *Toledo*
 Brandon J Erickson, *Chicago*
 Nathan Joseph Fanter, *Hines*
 Ashraf S Gorgey, *Richmond*
 Timothy August Hartshorn, *Manhattan Beach*
 John E Herzenberg, *Baltimore*
 Jake Paul Heiney, *Toledo*
 Matthew C Hoch, *Norfolk*
 Johanna Marie Hoch, *Norfolk*
 Mozammil Hussain, *Chesterfield*
 Pier Francesco Indelli, *Albuquerque*
 Michael Joseph, *Storrs*
 Srinath Kamineni, *Lexington*
 Eldin E Karaikovic, *Evanston*
 Jeffrey Bruce Knox, *Honolulu*
 Fatih Kucukdurmaz, *Philadelphia*
 Kevin Laudner, *Normal*
 KH Lee, *Rockville*
 Bingyun Li, *Morgantown*
 Xinning Li, *Boston*
 Zong-Ming Li, *Cleveland*
 Randall Loder, *Indianapolis*
 Mark Kevan Lyons, *Phoenix*
 Eleftherios A Makris, *Davis*
 Aditya Vikram Maheshwari, *Brooklyn*
 Paul David Metzger, *North Chicago*
 Subburaman Mohan, *Loma Linda*
 Arash Momeni, *Palo Alto*
 Freeman Miller, *Wilmington*
 Rahul Kumar Nath, *Houston*
 Ripul R Panchal, *Sacramento*
 Vinod Panchbhavi, *Galveston*
 Nikolaos K Paschos, *Davis*
 Ming Pei, *Morgantown*
 Shannon MBravo Petersen, *Des Moines*
 Matthew Robert Schmitz, *Fort Sam Houston*
 Bruce M Rothschild, *Indiana*
 Ran Schwarzkopf, *Orange*
 Jason Scott Scibek, *Pittsburgh*
 Shahin E Sheibani-Rad, *Los Angeles*
 Manish K Sethi, *Nashville*
 Vani Sabesan, *Dearborn*
 Kern Singh, *Chicago*
 William D Smith, *Las Vegas*
 Ettore Vulcano, *Baltimore*
 Ying-Chih Wang, *Milwaukee*
 Joshua T Weinhandl, *Norfolk*
 Charalampos Zalavras, *Los Angeles*
 Chunfeng Zhao, *Rochester*
 Nigel Zheng, *Charlotte*

MINIREVIEWS

- 776 Evaluation and treatment of internal impingement of the shoulder in overhead athletes
Corpus KT, Camp CL, Dines DM, Altchek DW, Dines JS
- 785 Lessons learned from study of congenital hip disease in adults
Hartofilakidis G, Lampropoulou-Adamidou K
- 793 Fifth metatarsal fractures and current treatment
Bowes J, Buckley R

ORIGINAL ARTICLE

Basic Study

- 801 Extrinsic visual feedback and additional cognitive/physical demands affect single-limb balance control in individuals with ankle instability
Hung Y, Miller J

Case Control Study

- 808 Benefits of the use of blood conservation in scoliosis surgery
Loughenbury PR, Berry L, Brooke BT, Rao AS, Dunsmuir RA, Millner PA

Retrospective Study

- 814 Windsurfing *vs* kitesurfing: Injuries at the North Sea over a 2-year period
van Bergen CJA, Commandeur JP, Weber RIK, Haverkamp D, Breederveld RS
- 821 Seasonal variation in adult hip disease secondary to osteoarthritis and developmental dysplasia of the hip
Sueyoshi T, Ritter MA, Davis KE, Loder RT

Observational Study

- 826 Effect of introducing an online system on the follow-up of elbow arthroplasty
Viveen J, Prkic A, The B, Koenraadt KLM, Eygendaal D
- 832 Surgical apgar score predicts early complication in transfemoral amputees: Retrospective study of 170 major amputations
Wied C, Foss NB, Kristensen MT, Holm G, Kallemose T, Troelsen A

CASE REPORT

- 839 Recurrent missense mutation of *GDF5* (*p.R438L*) causes proximal symphalangism in a British family
Leonidou A, Irving M, Holden S, Katchburian M

843 Glomus tumors of the fingers: Expression of vascular endothelial growth factor

Honsawek S, Kitidumrongsook P, Luangjarmekorn P, Pataradool K, Thanakit V, Patradul A

ABOUT COVER

Editorial Board Member of *World Journal of Orthopedics*, Sheng-Mou Hou, MD, MHSc, PhD, Professor, Department of Orthopedics, Shin Kong Wu Ho-Su Memorial Hospital, Taipei 11101, Taiwan

AIM AND SCOPE

World Journal of Orthopedics (*World J Orthop*, *WJO*, online ISSN 2218-5836, DOI: 10.5312) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJO covers topics concerning arthroscopy, evidence-based medicine, epidemiology, nursing, sports medicine, therapy of bone and spinal diseases, bone trauma, osteoarthropathy, bone tumors and osteoporosis, minimally invasive therapy, diagnostic imaging. Priority publication will be given to articles concerning diagnosis and treatment of orthopedic diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

We encourage authors to submit their manuscripts to *WJO*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Orthopedics is now indexed in PubMed, PubMed Central, and Scopus.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Shui Qiu*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Orthopedics

ISSN
 ISSN 2218-5836 (online)

LAUNCH DATE
 November 18, 2010

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Quanjun (Trey) Cui, MD, Professor, Department of Orthopaedic Surgery, School of Medicine, University of Virginia, Charlottesville, VA 22908, United States

Bao-Gan Peng, MD, PhD, Professor, Department of Spinal Surgery, General Hospital of Armed Police Force, 69 Yongding Road, Beijing 100039, China

EDITORIAL BOARD MEMBERS
 All editorial board members resources online at <http://www.wjgnet.com>

www.wjgnet.com/2218-5836/editorialboard.htm

EDITORIAL OFFICE
 Xiu-Xia Song, Director
 Fang-Fang Ji, Vice Director
World Journal of Orthopedics
 Baishideng Publishing Group Inc
 8226 Regency Drive, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: editorialoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 8226 Regency Drive,
 Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: bpgoffice@wjgnet.com
 Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>
<http://www.wjgnet.com>

PUBLICATION DATE
 December 18, 2016

COPYRIGHT
 © 2016 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.wjgnet.com/esps/>

Evaluation and treatment of internal impingement of the shoulder in overhead athletes

Keith T Corpus, Christopher L Camp, David M Dines, David W Altchek, Joshua S Dines

Keith T Corpus, Christopher L Camp, David M Dines, David W Altchek, Joshua S Dines, Shoulder and Sports Medicine Service, Hospital for Special Surgery, New York, NY 10021, United States

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: No potential conflicts of interest. No financial support.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Keith T Corpus, MD, Department of Academic Training, Shoulder and Sports Medicine Service, Hospital for Special Surgery, 535 E 70th Street, New York, NY 10021, United States. corpuske@hss.edu
Telephone: +1-312-6187775

Received: April 28, 2016

Peer-review started: April 28, 2016

First decision: May 17, 2016

Revised: September 14, 2016

Accepted: October 5, 2016

Article in press: October 7, 2016

Published online: December 18, 2016

Abstract

One of the most common pathologic processes seen in overhead throwing athletes is posterior shoulder

pain resulting from internal impingement. "Internal impingement" is a term used to describe a constellation of symptoms which result from the greater tuberosity of the humerus and the articular surface of the rotator cuff abutting the posterosuperior glenoid when the shoulder is in an abducted and externally rotated position. The pathophysiology in symptomatic internal impingement is multifactorial, involving physiologic shoulder remodeling, posterior capsular contracture, and scapular dyskinesis. Throwers with internal impingement may complain of shoulder stiffness or the need for a prolonged warm-up, decline in performance, or posterior shoulder pain. On physical examination, patients will demonstrate limited internal rotation and posterior shoulder pain with a posterior impingement test. Common imaging findings include the classic "Bennett lesion" on radiographs, as well as articular-sided partial rotator cuff tears and concomitant SLAP lesions. Mainstays of treatment include intense non-operative management focusing on rest and stretching protocols focusing on the posterior capsule. Operative management is variable depending on the exact pathology, but largely consists of rotator cuff debridement. Outcomes of operative treatment have been mixed, therefore intense non-operative treatment should remain the focus of treatment.

Key words: Internal impingement; Overhead athlete; Partial rotator cuff tear; Scapular dyskinesis; Posterior capsular contracture; SLAP tear

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: "Internal impingement" is a term used to describe a constellation of symptoms which result from the greater tuberosity of the humerus and the articular surface of the rotator cuff abutting the posterosuperior glenoid when the shoulder is in an abducted and externally rotated position. The pathophysiology in symptomatic internal impingement is multifactorial, involving physiologic shoulder remodeling, posterior

capsular contracture, and scapular dyskinesis. Mainstays of treatment include intense non-operative management focusing on rest and stretching protocols focusing on the posterior capsule.

Corpus KT, Camp CL, Dines DM, Altchek DW, Dines JS. Evaluation and treatment of internal impingement of the shoulder in overhead athletes. *World J Orthop* 2016; 7(12): 776-784 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/776.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.776>

INTRODUCTION

Overhead throwing athletes, in particular baseball players, often place unique and significant repetitive stresses across the shoulder at the extremes of the functional arc of motion^[1]. Over the course of a career, repeated loading can lead to osseous and soft-tissue changes and ultimately pathology of the shoulder girdle^[2-6]. The complex biomechanics of the elite thrower predispose them to multiple types of shoulder dysfunction, and these patients often serve as a clinical challenge for the sports medicine physician.

One of the most common pathologic processes seen in this patient population is shoulder pain resulting from internal impingement. "Internal impingement" is a term used to describe a constellation of symptoms which result from the greater tuberosity of the humerus and the articular surface of the rotator cuff abutting the posterosuperior glenoid when the shoulder is in an abducted and externally rotated position^[7].

The purpose of this article is to review the patho-anatomic features of symptomatic internal impingement, as well as review the current concepts involved with diagnosis and treatment of this condition.

HISTORICAL PERSPECTIVE

Posterior shoulder pain has been a debated topic dating back to the 1950s, as described by Bennett^[8]. At that time, he proposed that pain in the posterior shoulder was secondary to inflammation in the posterior capsule and inferior glenohumeral ligament due to triceps traction. This traction injury resulted in exostosis of the posteroinferior glenoid rim, which became known as the "Bennett lesion"^[8]. Bennett also described the presence of articular-sided posterosuperior rotator cuff tears in these same athletes^[9]. In 1977, Lombardo *et al.*^[10] further described ossification of the posterior glenoid rim in their description of an open approach for treatment of posterior shoulder pain in overhead throwing athletes.

In 1985, Andrews *et al.*^[11] described a series of overhead athletes with posterior shoulder pain that developed articular-sided posterosuperior cuff tears with concomitant SLAP lesions. Later, Jobe *et al.*^[12] reported on a series of overhead athletes with posterosuperior impingement associated with anterior instability. They

found that these patients did not respond well to standard subacromial decompression, but rather had success with anterior capsulolabral reconstruction. In addition, these patients often presented with a number of associated injuries including superior or inferior labral tears, rotator cuff tears, injury to the greater tuberosity or glenoid, or inferior glenohumeral ligament injury.

In 1992, Walch *et al.*^[7] reported a series of patients with impingement between the articular side of the supraspinatus tendon and the posterosuperior edge of the glenoid cavity, typically noted during maximal abduction and external rotation. At arthroscopy, these patients classically demonstrated a partial articular-sided rotator cuff tear. As a result, they described the "internal impingement" mechanism in which the undersurface of the posterior rotator cuff becomes entrapped between the labrum and the greater tuberosity in the abduction-external rotation position^[7,13].

PATHOPHYSIOLOGY AND BIOMECHANICS

The biomechanical pathogenesis of internal impingement has been widely debated since its description. Some had posited that acquired anterior instability is the causative factor, while others have refuted this notion citing evidence suggesting no correlation between symptomatic internal impingement and anterior glenohumeral translation^[12,14-20]. More current thinking suggests that symptomatic internal impingement is multifactorial, involving physiologic shoulder remodeling, posterior capsular contracture, and scapular dyskinesis^[21,22].

Kinetic chain

The kinetic chain concept describes the coordinated motion that transmits energy in a synchronized fashion from the lower extremity, through the trunk, to the shoulder, and finally to the ball as it is released^[23-25]. Key elements of the kinetic chain are leg strength, body rotation, core strength, scapular position and motion, and shoulder rotation. Inflexibility, weakness, and imbalance of any point in the kinetic chain can create a situation where the arm lags behind the legs and trunk, placing the throwing shoulder in a vulnerable position, increasing stresses about the shoulder and leading to injury.

This concept is vital to the throwing motion and has been broken down into six distinct phases which comprise the throwing cycle. The first three phases consist of the wind-up, early cocking, and late cocking phases. These phases account for the bulk of the total time spent in the throwing motion (approximately 1.5 s), and they allow proper positioning of the lower extremities, core, and arms in preparation for release of the ball^[15,26,27]. In the late cocking phase, the shoulder is placed in abduction (90-100 degrees) and maximal external rotation (170-180 degrees), the position commonly associated with internal impingement^[7]. The fourth phase, the acceleration phase, is the phase in which the greatest angular velocity change

is seen across the shoulder joint as the ball is propelled forward. This motion occurs at a rotational velocity of over 7250 degrees per second and is the fastest human motion to ever be recorded^[24,28-30]. It follows that this phase results in the most injuries, despite being the shortest phase (0.05 s). As the ball is released, the deceleration phase and follow through phase are completed which result in a distraction force across the joint as the arm is slowed (0.35 s).

Thrower's paradox

The "thrower's paradox" refers to the delicate balance between mobility and stability which allows pitchers to achieve a high level of function^[24,31]. To generate rotational velocities upwards of 7000°/s, the arc of motion must be expanded to allow maximal external rotation of the shoulder. The normal arc of rotation of a healthy shoulder from maximal internal rotation to maximal external rotation is 180°^[31]. The arc of motion in a high-level throwing athlete is shifted posteriorly to allow for increased external rotation at the cost of decreased internal rotation by allowing increased clearance of the greater tuberosity over the glenoid during rotation^[2-4,21,23,25]. Increased external rotation is achieved by a number of shoulder adaptations that develop over time including increased retroversion of the humeral head and glenoid, and increased anterior capsular laxity^[1,2,4,5,17,32].

Andrews *et al.*^[33] and Bigliani *et al.*^[34] have suggested that glenohumeral joint laxity is a common finding among throwing athletes. Jobe *et al.*^[12,32,35] originally described "subtle instability", or microinstability, to define the acquired laxity and anterior translation of the humeral head that occurs with the arm in a maximally abducted and externally rotated position. At what point this laxity becomes pathologic is another matter of debate. Subtle instability is postulated to result from repetitive shear stresses during the cocking and acceleration phases and contributes to the development of labral tears and articular-sided rotator cuff tears. Paley *et al.*^[17] stated anterior instability is actually the most significant factor in the development of internal impingement.

Alternatively, some authors have posited that micro-instability of the shoulder actually protects against internal impingement^[3,7,21]. Cadaveric, magnetic resonance imaging (MRI), and arthroscopic studies have consistently shown that contact of the rotator cuff on the posterosuperior labrum is a normal, physiologic occurrence^[3,21,23,28]. This theory postulates that the abnormal laxity of the humerus relative to the glenoid actually prevents impingement between the greater tuberosity and superior glenoid.

The anatomic changes allowing for increased external rotation can also result in remodeling of the posterior soft tissues, leading to contracture of the posterior capsule and posterior band of the inferior glenohumeral ligament^[21]. This increased external rotation creates increased torsional and shear stress upon the biceps anchor and undersurface of the rotator cuff^[1,7,28,32,35,36].

Despite the need for increased laxity, adequate stability must be maintained to prevent symptomatic humeral head subluxation, often achieved through further posterior capsular contracture. When present, these alterations can contribute to internal impingement and lead to rotator cuff tears, labral tears, capsular injuries, chondral injuries, and biceps tendon pathology. These findings were confirmed in a cadaveric model by Grossman *et al.*^[26], who reported on a simulated posterior capsular contraction model which led to GIRD and posterosuperior translation of the humeral head during the late cocking, ultimately resulting in SLAP injuries. Each of these processes can lead to pain, decreased velocity, loss of control, and diminished endurance in the throwing athlete.

Clinically, loss of 15 degrees or more of internal rotation in the throwing shoulder compared to the non-dominant arm is commonly seen. The potential for injury increases once this threshold has been reached. Burkhart *et al.*^[21,37] have reported that shoulders with an internal rotation deficit > 25 degrees are at increased risk for development of SLAP lesions as a result of increased posterosuperior peel back on the labrum. In addition, Dines *et al.*^[38] have shown that throwers with ulnar collateral ligament insufficiency at the elbow demonstrated a significant amount of GIRD as compared to players without a history of elbow injury.

Scapular dyskinesia

Kibler^[39] has defined scapular dyskinesia as an alteration in the normal resting position of the scapula or an alteration in the normal dynamic scapular motion. The scapula serves as an important link in the kinetic chain. When the scapula is unable to effectively transmit energy from the trunk to the pitching arm or stabilize the shoulder properly, pitching mechanics become inefficient and pitching velocity can suffer. Pitchers will then compensate by recruiting other surrounding musculature and increasing stress across the shoulder joint^[39].

Scapular motion has been found to be more intricate than once thought. Instead of the proposed 2:1 ratio of humeral to scapular motion during forward elevation, recent studies have shown the scapula to have a more complex role in shoulder motion. Scapular motion is now defined in three planes: Internal/external rotation around a vertical axis, upward/downward rotation around a horizontal axis, and anterior/posterior tilt around a horizontal axis^[39]. The intricate scapular positioning is controlled dynamically by force couples generated by the trapezius, serratus anterior, latissimus dorsi, and rhomboid musculature. These muscular couples contract before rotator cuff activation, allowing the cuff to contract against a stable scapular base^[40].

Myers *et al.*^[41] have previously reported that throwers normally develop upward rotation, internal rotation, and retraction of the scapula during forward elevation of the humerus. Scapular dyskinesia may result from inflexibility or imbalances in periscapular muscles secondary to fatigue, direct trauma, or nerve injury^[25].

Table 1 Keys to diagnosing internal impingement

History	Shoulder stiffness Need for prolonged warm-up Decline in performance (loss of velocity of control)
Physical exam	Posterior shoulder pain in late cocking phase Posterior glenohumeral joint line tenderness Increased external rotation, decreased internal rotation Scapular dyskinesia Positive anterior relocation test
Imaging	Positive posterior impingement sign Bennett lesion (exostosis of posteroinferior glenoid rim) Sclerosis of greater tuberosity, posterior humeral head cysts, rounding of posterior glenoid rim Posterosuperior labral tears Partial-thickness articular-sided rotator cuff tears (supraspinatus, infraspinatus)

Table 2 Jobe's clinical classification of internal impingement^[35]

Stage	Presentation/symptoms
I : Early	Shoulder stiffness and need for prolonged warm-up, no pain with ADLs
II : Intermediate	Pain localized to the posterior shoulder in the late cocking phase, no pain with ADLs
III : Advanced	Similar symptoms to Stage II, but refractory to a period of adequate rest and rehabilitation

ADL: Activities of daily living.

In pitchers with poor scapulothoracic rhythm, there is a trend toward scapular internal rotation and protraction around the rib cage resulting from inflexibility or imbalances in the periscapular musculature^[41]. When the scapula is ineffective in stabilizing the shoulder, the rotator cuff is forced to over-compensate to stabilize the glenohumeral joint. These loads are then transmitted to the superior glenoid and the articular surface of the rotator cuff tendons and can lead to injury. This alteration in function is thought to be an independent factor in the development of internal impingement. It follows that scapular dyskinesia has been reported in up to 100% of patients with internal impingement^[40,42].

HISTORY AND PHYSICAL EXAMINATION

A thorough history is the first step in appropriately diagnosing internal impingement (Table 1). Throwers with internal impingement may complain of shoulder stiffness or the need for a prolonged warm-up. They may also note a decline in performance, including loss of control or decreases in pitch velocity. They may also describe posterior shoulder pain, especially in the late cocking phase. These complaints were outlined by Jobe^[35], who defined three stages in the clinical presentation of internal impingement. Stage I consists of stiffness and difficulty in warming up, but no complaints of pain. Stage II is hallmarked by the complaint of pain during the late cocking phase of the throwing cycle. Those patients that have recurrent pain after a period of adequate rest and rehabilitation are classified as Stage III (Table 2).

The classic presentation and physical exam findings in the throwing shoulder with internal impingement commonly consists of posterior glenohumeral joint line tenderness, increased external rotation, and decreased

internal rotation. Despite this common pattern, a complete and thorough physical exam is important to identify any other associated shoulder pathology. The exam should start with visual inspection. Inspection may demonstrate greater muscular development in the dominant extremity, but assessment for any muscular atrophy must be performed. The scapulae are evaluated for positioning, dyskinesia, and winging. The scapula may have a prominent inferior medial border, and the throwing shoulder may appear to sag inferiorly compared to the non-throwing shoulder. Next, the coracoid process, anterior and posterior joint lines, greater tuberosity, long head of biceps tendon, AC joint, and deltoid should be palpated for tenderness.

Rotational glenohumeral motion should be assessed with the arm at the side and at 90 degrees of abduction. Internal impingement typically leads to posterior shoulder tightness in the throwing shoulder, leading to a loss of internal rotation^[4,43]. This finding has been confirmed in a population of college baseball players with shoulder pain, who demonstrated a 10 degree loss of internal rotation in their throwing shoulder as compared to both their non-dominant shoulder and pain-free controls^[44]. Forward elevation and horizontal abduction should also be evaluated.

Strength examination focusing the rotator cuff should be completed in all patients with suspected internal impingement. Rotator cuff involvement can range from undersurface fraying, to partial articular-sided tears, to full-thickness tears. The most common tendon involved is usually the infraspinatus; therefore special attention should be paid to external rotation strength.

Special testing may include the relocation test, described by Jobe, in which the shoulder is placed in 90 degrees of abduction and maximal external rotation.



Figure 1 Magnetic resonance image of Bennett lesion and corresponding arthroscopic picture viewing posteriorly from anterosuperior portal.

While in this position, the humerus is loaded in both an anterior and posterior direction. While posterior directed force will provoke pain and impingement, anterior loads will relieve pain (opposite from the traditional findings in patients with anterior shoulder instability)^[35]. A second test, the posterior impingement sign, was described by Meister^[45] and involves placing the shoulder into 90 to 110 degrees of abduction, slight extension, and maximum external rotation. The provocation of deep posterior pain indicates a positive test and is highly correlated with undersurface tearing of the rotator cuff and/or posterior labrum.

In addition to the relocation test described above, a global stability exam is also important in the evaluation of internal impingement. The difficulty with stability examination in this patient population harkens back to the “thrower’s paradox” previously described. Many of these patients have adaptive laxity, which must be distinguished from pathologic laxity. Most often, the most important finding is the patient’s subjective sensation of shoulder subluxation during examination, which may occur while placing the patient in the position of apprehension. Additionally, a good examination under anesthesia at arthroscopy is vital for stability testing.

Lastly, examination of the posterosuperior labrum is an important component of the internal impingement exam, as labral tears in this location are common. Multiple physical exam maneuvers have been described for evaluation of the superior labrum and have shown high sensitivity for detection of tears, but none have shown high specificity for identification of superior labral tears^[46-48].

RADIOGRAPHIC EVALUATION

Radiographic evaluation should begin with standard shoulder radiographs, including internal and external rotation anteroposterior, scapular Y, axillary, and West Point views^[1]. Radiographs may be normal in the setting of internal impingement, but patients may display several radiographic findings in association with this pathologic process. Common radiographic findings include the “Bennett lesion” (exostosis of the posteroinferior glenoid rim), sclerosis of the greater tuberosity, posterior humeral

head osteochondral cysts, and rounding of the posterior glenoid rim^[8,9].

The mainstay of radiographic evaluation is MRI, which has a high sensitivity for capsular, labral, and rotator cuff pathology in the throwing shoulder. At our institution, we routinely perform noncontrast MRI, as it has been shown to have equivalent or superior sensitivity and specificity rates to MR arthrogram, when appropriate pulse sequences are utilized^[49]. Common MRI findings in patients with internal impingement include posterosuperior labral tears, partial-thickness articular-sided rotator cuff tears most notably at the junction between the supraspinatus and infraspinatus as they insert on to the humeral head, and cystic changes in the posterior aspect of the humeral head^[50,51]. Additionally, patients can display calcification at the scapular attachment of the posterior capsule (Bennett lesion), posterior capsular contracture and thickening at the level of the posterior band of the inferior glenohumeral ligament, and subchondral fracture and remodeling of the posterosuperior glenoid^[1] (Figures 1-3).

TREATMENT

Nonoperative management

Once a diagnosis of internal impingement is made, non-operative management should be recommended as the first line treatment. The proper non-operative treatment can be tailored based on stages set forth by Jobe discussed earlier^[35]. Patients in Stage I (those with complaints of stiffness and difficulty warming up but without localized posterior shoulder pain) should be prescribed a course of nonsteroidal anti-inflammatories and rest. Patients in Stage II (those with isolated posterior shoulder pain) usually require four to six weeks of rest and can also benefit from physical therapy^[1]. Physical therapy has been shown to be both therapeutic and protective against further injury in several studies^[21,22,31].

Given the pathophysiologic mechanism of internal impingement, therapy is focused on correction of aberrant shoulder range of motion and scapular dyskinesis. To that end, special attention should be paid to correction of GIRD through the “sleeper stretch” which allows posterior

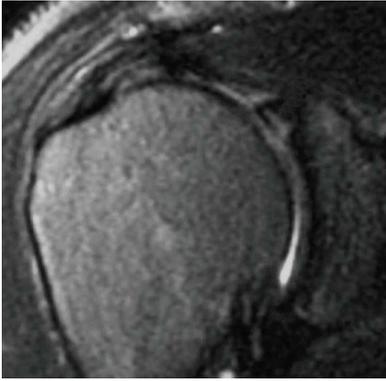


Figure 2 Magnetic resonance image of a Type 2 SLAP tear with concomitant partial thickness rotator cuff tear.



Figure 3 Partial thickness articular-sided tear of infraspinatus as viewed from posterior portal.

capsular stretching. In a study of high-level tennis players performing daily “sleeper stretch” exercises, patients were found to have significant increases in both internal rotation and total rotation, as well as a 38% decrease in the prevalence of shoulder problems^[21] (Figure 4). In addition, scapular stabilization exercises should be recommended. As the throwing motion involves the entire body through the kinetic chain, core strengthening and lower body strengthening must also be stressed simultaneously. Lastly, proper throwing mechanics should be enforced, especially for younger athletes.

Corticosteroid injections directed at the posteroinferior glenoid rim have been described^[52]. These injections have mostly been used for diagnostic, rather than therapeutic, purposes. To this point, no compelling data has been published to support injections for internal impingement and should be used judiciously due to the potential risk of permanent tendon damage.

Operative treatment

Due to the spectrum of pathology seen in internal impingement, multiple operative treatment options exist. Paley *et al.*^[17] published a series demonstrating > 80% incidence of concomitant articular-sided rotator cuff tear in professional overhead athletes with internal impingement. Often, this tear will be associated with an adjacent “kissing



Figure 4 Demonstration of the “sleeper stretch”.

lesion” seen as a labral tear. Historically, treatment of these lesions has included debridement or repair and possible acromioplasty, with mixed results. Andrews *et al.*^[11] published a series of thirty-six overhead athletes with articular-sided partial tears of the supraspinatus that underwent arthroscopic debridement. They found 85% were able to return to their pre-morbid level of function, which they attributed to stimulation of tendon healing *via* debridement. Similarly, Sonnery-Cottet *et al.*^[20] performed arthroscopic debridement on twenty-eight tennis players with articular-sided partial tears and glenoid lesions. Seventy-nine percent were able to return to play, but 91% still had some persistent pain.

Historically, most surgeons have felt that lesions involving more than half of the thickness of a rotator cuff tendon should be repaired. Some authors support completion of these partial tears to aid in soft-tissue mobilization, followed by standard double-row repair^[53-55]. More recent data suggests that partial tears up to 75% in high-level throwing athletes should be debrided unless they involve the anterior cable of the rotator cuff. The high forces that throwing athletes generate subject the cuff to intense stress and threaten the repair integrity^[56]. In cases involving injury to the anterior cable, the anterior cable can be repaired and the partial thickness posterior cuff injury can be debrided. If partial tear completion and repair is indicated, a lateralized double-row repair as described by Dines *et al.*^[57], should be considered as it has shown favorable outcomes in professional overhead throwing athletes, allowing restoration of a more anatomic footprint.

Additional pathology seen in internal impingement includes SLAP tears, biceps tenosynovitis, and degenerative changes in the humeral articular surface^[7,58]. Meister *et al.*^[45] reported their results of twenty-two overhead athletes with internal impingement who underwent debridement of the rotator cuff, biceps, and labrum. A subset of patients also underwent arthroscopic removal of a Bennett lesion. Only 55% of the cohort had returned to their pre-morbid level at 6 years post-op. Neri *et al.*^[59] also evaluated a cohort of high-level overhead athletes who underwent Type II SLAP repairs at a mean of three years follow up and found that only 57% were able to

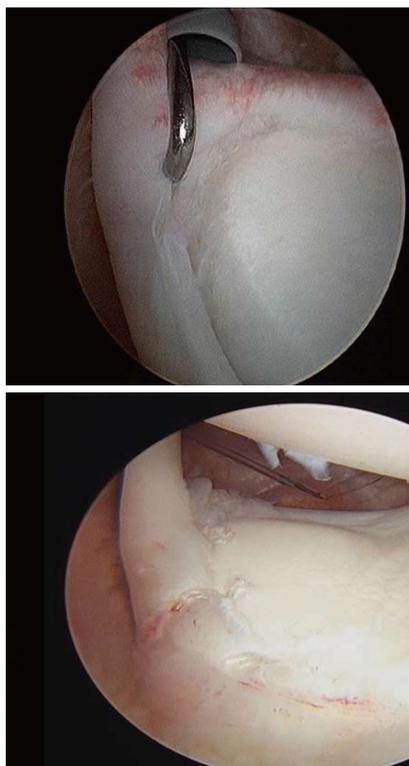


Figure 5 Type 2B SLAP tear s/p repair.

return to their pre-injury level of competition, while an additional 25% returned to sport but were limited by pain. These marginal results may be due to the higher demand elite overhead athletes place on their shoulders and higher expectations amongst the study group. In addition, Neri *et al*^[59] showed that a statistically significant correlation did exist between the presence of partial-thickness rotator cuff tears and the inability to return to pre-injury level of play (Figure 5).

Andrews *et al*^[60] have suggested that the poor results of debridement alone could be attributed to unaddressed subtle anterior laxity. As a result, they advocated for concomitant open anterior stabilization. They reported a 92% success rate at an average of close to three years postoperatively in a cohort of twenty-five athletes. Other studies have had less-optimistic results^[35].

Lastly, some authors have proposed osseous procedures to address the osseous changes which heavily contribute process of internal impingement. Riand *et al*^[61] reported on humeral osteotomies to increase humeral retroversion in twenty patients who had continued pain after arthroscopic debridement. Eleven of the twenty patients were able to resume sports activities at the same level, and five were able to resume sports at a lower level.

CONCLUSION

Internal impingement is a complex pathologic process secondary to repetitive use in overhead athletes resulting in articular-sided partial-thickness rotator cuff tears and

SLAP lesions. The pathogenesis of internal impingement is multi-factorial. Understanding the etiology and pathogenesis will allow proper diagnosis and treatment.

REFERENCES

- 1 **Drakos MC**, Rudzki JR, Allen AA, Potter HG, Altchek DW. Internal impingement of the shoulder in the overhead athlete. *J Bone Joint Surg Am* 2009; **91**: 2719-2728 [PMID: 19884449 DOI: 10.2106/JBJS.I.00409]
- 2 **Crockett HC**, Gross LB, Wilk KE, Schwartz ML, Reed J, O' Mara J, Reilly MT, Dugas JR, Meister K, Lyman S, Andrews JR. Osseous adaptation and range of motion at the glenohumeral joint in professional baseball pitchers. *Am J Sports Med* 2002; **30**: 20-26 [PMID: 11798991]
- 3 **Halbrecht JL**, Tirman P, Atkin D. Internal impingement of the shoulder: comparison of findings between the throwing and non-throwing shoulders of college baseball players. *Arthroscopy* 1999; **15**: 253-258 [PMID: 10231101 DOI: 10.1016/S0749-8063(99)70030-7]
- 4 **Myers JB**, Laudner KG, Pasquale MR, Bradley JP, Lephart SM. Glenohumeral range of motion deficits and posterior shoulder tightness in throwers with pathologic internal impingement. *Am J Sports Med* 2006; **34**: 385-391 [PMID: 16303877 DOI: 10.1177/0363546505281804]
- 5 **Osahr DC**, Cannon DL, Speer KP. Retroversion of the humerus in the throwing shoulder of college baseball pitchers. *Am J Sports Med* 2002; **30**: 347-353 [PMID: 12016074]
- 6 **Wright RW**, Paletta GA. Prevalence of the Bennett lesion of the shoulder in major league pitchers. *Am J Sports Med* 2004; **32**: 121-124 [PMID: 14754734 DOI: 10.1177/0363546503260712]
- 7 **Walch G**, Boileau P, Noel E, Donell ST. Impingement of the deep surface of the supraspinatus tendon on the posterosuperior glenoid rim: An arthroscopic study. *J Shoulder Elbow Surg* 1992; **1**: 238-245 [PMID: 22959196 DOI: 10.1016/S1058-2746(09)80065-7]
- 8 **Bennett GE**. Shoulder and elbow lesions distinctive of baseball players. 1947. *Clin Orthop Relat Res* 2012; **470**: 1531-1533 [PMID: 22476897 DOI: 10.1007/s11999-012-2335-2]
- 9 **Bennett GE**. Elbow and shoulder lesions of baseball players: George E. Bennett MD (1885-1962). The 8th president of the AAOS 1939. *Clin Orthop Relat Res* 2008; **466**: 62-73 [PMID: 18196375 DOI: 10.1007/s11999-007-0028-z]
- 10 **Lombardo SJ**, Jobe FW, Kerlan RK, Carter VS, Shields CL. Posterior shoulder lesions in throwing athletes. *Am J Sports Med* 1977; **5**: 106-110 [PMID: 860772 DOI: 10.1177/03635465770050302]
- 11 **Andrews JR**, Broussard TS, Carson WG. Arthroscopy of the shoulder in the management of partial tears of the rotator cuff: a preliminary report. *Arthroscopy* 1985; **1**: 117-122 [PMID: 4091915 DOI: 10.1016/S0749-8063(85)80041-4]
- 12 **Jobe FW**, Kvitne RS, Giangarra CE. Shoulder pain in the overhand or throwing athlete. The relationship of anterior instability and rotator cuff impingement. *Orthop Rev* 1989; **18**: 963-975 [PMID: 2797861]
- 13 **Walch G**, Liotard JP, Boileau P, Noël E. [Postero-superior glenoid impingement. Another impingement of the shoulder]. *J Radiol* 1993; **74**: 47-50 [PMID: 8483151]
- 14 **Conway JE**. Arthroscopic repair of partial-thickness rotator cuff tears and SLAP lesions in professional baseball players. *Orthop Clin North Am* 2001; **32**: 443-456 [PMID: 11888139]
- 15 **Jobe FW**, Moynes DR, Tibone JE, Perry J. An EMG analysis of the shoulder in pitching. A second report. *Am J Sports Med* 1984; **12**: 218-220 [PMID: 6742305]
- 16 **Kvitne RS**, Jobe FW. The diagnosis and treatment of anterior instability in the throwing athlete. *Clin Orthop Relat Res* 1993; **107**-123 [PMID: 8504590]
- 17 **Paley KJ**, Jobe FW, Pink MM, Kvitne RS, ElAttrache NS. Arthroscopic findings in the overhand throwing athlete: evidence for posterior internal impingement of the rotator cuff. *Arthroscopy* 2000; **16**: 35-40 [PMID: 10627343 DOI: 10.1016/

- S0749-8063(00)90125-7]
- 18 **Borsa PA**, Wilk KE, Jacobson JA, Scibek JS, Dover GC, Reinold MM, Andrews JR. Correlation of range of motion and glenohumeral translation in professional baseball pitchers. *Am J Sports Med* 2005; **33**: 1392-1399 [PMID: 16002489 DOI: 10.1177/0363546504273490]
 - 19 **Ellenbecker TS**, Mattalino AJ, Elam E, Caplinger R. Quantification of anterior translation of the humeral head in the throwing shoulder. Manual assessment versus stress radiography. *Am J Sports Med* 2000; **28**: 161-167 [PMID: 10750991]
 - 20 **Sonnery-Cottet B**, Edwards TB, Noel E, Walch G. Results of arthroscopic treatment of posterosuperior glenoid impingement in tennis players. *Am J Sports Med* 2002; **30**: 227-232 [PMID: 11912093]
 - 21 **Burkhart SS**, Morgan CD, Kibler WB. The disabled throwing shoulder: spectrum of pathology Part I: pathoanatomy and biomechanics. *Arthroscopy* 2003; **19**: 404-420 [PMID: 12671624 DOI: 10.1053/jars.2003.50128]
 - 22 **Burkhart SS**, Morgan CD, Kibler WB. The disabled throwing shoulder: spectrum of pathology Part III: The SICK scapula, scapular dyskinesis, the kinetic chain, and rehabilitation. *Arthroscopy* 2003; **19**: 641-661 [PMID: 12861203 DOI: 10.1016/S0749-8063(03)00389-X]
 - 23 **Edelson G**, Teitz C. Internal impingement in the shoulder. *J Shoulder Elbow Surg* 2000; **9**: 308-315 [PMID: 10979527 DOI: 10.1067/mse.2000.105449]
 - 24 **Fleisig GS**, Andrews JR, Dillman CJ, Escamilla RF. Kinetics of baseball pitching with implications about injury mechanisms. *Am J Sports Med* 1995; **23**: 233-239 [PMID: 7778711 DOI: 10.1177/036354659502300218]
 - 25 **Braun BS**, Kokmeyer D, Millett PJ. Shoulder injuries in the throwing athlete. *Bone* 2011; **91**: 966-978 [DOI: 10.2106/JBJS.H.01341]
 - 26 **Grossman MG**, Tibone JE, McGarry MH, Schneider DJ, Veneziani S, Lee TQ. A cadaveric model of the throwing shoulder: a possible etiology of superior labrum anterior-to-posterior lesions. *J Bone Joint Surg Am* 2005; **87**: 824-831 [PMID: 15805213 DOI: 10.2106/JBJS.D.01972]
 - 27 **Kelly BT**, Backus SI, Warren RF, Williams RJ. Electromyographic analysis and phase definition of the overhead football throw. *Am J Sports Med* 2002; **30**: 837-844 [PMID: 12435650 DOI: 10.1177/03635465020300061401]
 - 28 **Burkhart SS**. Internal impingement of the shoulder. *Instr Course Lect* 2006; **55**: 29-34 [PMID: 16958436]
 - 29 **Kuhn JE**, Lindholm SR, Huston LJ, Soslowky LJ, Blasier RB. Failure of the biceps superior labral complex: a cadaveric biomechanical investigation comparing the late cocking and early deceleration positions of throwing. *Arthroscopy* 2003; **19**: 373-379 [PMID: 12671620 DOI: 10.1053/jars.2003.50044]
 - 30 **Levitz CL**, Dugas J, Andrews JR. The use of arthroscopic thermal capsulorrhaphy to treat internal impingement in baseball players. *Arthroscopy* 2001; **17**: 573-577 [PMID: 11447542 DOI: 10.1053/jars.2001.24853]
 - 31 **Wilk KE**, Meister K, Andrews JR. Current concepts in the rehabilitation of the overhead throwing athlete. *Am J Sports Med* 2002; **30**: 136-151 [PMID: 11799012 DOI: 10.1177/0363546506290403]
 - 32 **Jobe CM**. Posterior superior glenoid impingement: expanded spectrum. *Arthroscopy* 1995; **11**: 530-536 [PMID: 8534293 DOI: 10.1016/0749-8063(95)90128-0]
 - 33 **Andrews JR**, Carson WG, McLeod WD. Glenoid labrum tears related to the long head of the biceps. *Am J Sports Med* 1985; **13**: 337-341 [PMID: 4051091 DOI: 10.1177/036354658501300508]
 - 34 **Bigliani LU**, Codd TP, Connor PM, Levine WN, Littlefield MA, Hershon SJ. Shoulder motion and laxity in the professional baseball player. *Am J Sports Med* 1997; **25**: 609-613 [PMID: 9302464 DOI: 10.1177/036354659702500504]
 - 35 **Jobe CM**. Superior glenoid impingement. *Orthop Clin North Am* 1997; **28**: 137-143 [PMID: 9113710]
 - 36 **Heyworth BE**, Williams RJ. Internal impingement of the shoulder. *Am J Sports Med* 2009; **37**: 1024-1037 [PMID: 19059895 DOI: 10.1177/0363546508324966]
 - 37 **Burkhart SS**, Morgan CD. The peel-back mechanism: its role in producing and extending posterior type II SLAP lesions and its effect on SLAP repair rehabilitation. *Arthroscopy* 1998; **14**: 637-640 [PMID: 9754487 DOI: 10.1016/S0749-8063(98)70065-9]
 - 38 **Dines JS**, Frank JB, Akerman M, Yocum LA. Glenohumeral internal rotation deficits in baseball players with ulnar collateral ligament insufficiency. *Am J Sports Med* 2009; **37**: 566-570 [PMID: 19059890 DOI: 10.1177/0363546508326712]
 - 39 **Kibler WB**. Scapular involvement in impingement: signs and symptoms. *Instr Course Lect* 2006; **55**: 35-43 [PMID: 16958437]
 - 40 **Kibler WB**. The role of the scapula in athletic shoulder function. *Am J Sports Med* 1998; **26**: 325-337 [PMID: 9548131 DOI: 10.1177/03635465980260022801]
 - 41 **Myers JB**, Laudner KG, Pasquale MR, Bradley JP, Lephart SM. Scapular position and orientation in throwing athletes. *Am J Sports Med* 2005; **33**: 263-271 [PMID: 15701613 DOI: 10.1177/0363546504268138]
 - 42 **Warner JJ**, Micheli LJ, Arslanian LE, Kennedy J, Kennedy R. Scapulothoracic motion in normal shoulders and shoulders with glenohumeral instability and impingement syndrome. A study using Moiré topographic analysis. *Clin Orthop Relat Res* 1992; **(285)**: 191-199 [PMID: 1446436]
 - 43 **Lintner D**, Mayol M, Uzodinma O, Jones R, Labossiere D. Glenohumeral internal rotation deficits in professional pitchers enrolled in an internal rotation stretching program. *Am J Sports Med* 2007; **35**: 617-621 [PMID: 17293473 DOI: 10.1177/0363546506296736]
 - 44 **Ruotolo C**, Price E, Panchal A. Loss of total arc of motion in collegiate baseball players. *J Shoulder Elbow Surg* 2006; **15**: 67-71 [PMID: 16414471 DOI: 10.1016/j.jse.2005.05.006]
 - 45 **Meister K**, Buckley B, Batts J. The posterior impingement sign: diagnosis of rotator cuff and posterior labral tears secondary to internal impingement in overhand athletes. *Am J Orthop (Belle Mead NJ)* 2004; **33**: 412-415 [PMID: 15379239]
 - 46 **Meserve BB**, Cleland JA, Boucher TR. A meta-analysis examining clinical test utility for assessing superior labral anterior posterior lesions. *Am J Sports Med* 2009; **37**: 2252-2258 [PMID: 19095895 DOI: 10.1177/0363546508325153]
 - 47 **O'Brien SJ**, Pagnani MJ, Fealy S, McGlynn SR, Wilson JB. The active compression test: a new and effective test for diagnosing labral tears and acromioclavicular joint abnormality. *Am J Sports Med* 1998; **26**: 610-613 [PMID: 9784804 DOI: 10.1177/03635465980260050201]
 - 48 **Parentis MA**, Glousman RE, Mohr KS, Yocum LA. An evaluation of the provocative tests for superior labral anterior posterior lesions. *Am J Sports Med* 2006; **34**: 265-268 [PMID: 16219944 DOI: 10.1177/0363546505279911]
 - 49 **Connell DA**, Potter HG, Wickiewicz TL, Altchek DW, Warren RF. Noncontrast magnetic resonance imaging of superior labral lesions. 102 cases confirmed at arthroscopic surgery. *Am J Sports Med* 1999; **27**: 208-213 [PMID: 10102103]
 - 50 **Kaplan LD**, McMahon PJ, Towers J, Irrgang JJ, Rodosky MW. Internal impingement: findings on magnetic resonance imaging and arthroscopic evaluation. *Arthroscopy* 2004; **20**: 701-704 [PMID: 15346111 DOI: 10.1016/j.arthro.2004.06.006]
 - 51 **Giaroli EL**, Major NM, Higgins LD. MRI of internal impingement of the shoulder. *AJR Am J Roentgenol* 2005; **185**: 925-929 [PMID: 16177410 DOI: 10.2214/AJR.04.0971]
 - 52 **Yoneda M**, Nakagawa S, Hayashida K, Fukushima S, Wakitani S. Arthroscopic removal of symptomatic Bennett lesions in the shoulders of baseball players: arthroscopic Bennett-plasty. *Am J Sports Med* 2002; **30**: 728-736 [PMID: 12239010]
 - 53 **Mithofer K**, Fealy S, Altchek DW. Arthroscopic treatment of internal impingement of the shoulder. *Tech Shoulder Elb Surg* 2004; **5**: 66-75
 - 54 **Lo IK**, Burkhart SS. Double-row arthroscopic rotator cuff repair: re-establishing the footprint of the rotator cuff. *Arthroscopy* 2003; **19**: 1035-1042 [PMID: 14608329]

- 55 **Meier SW**, Meier JD. Rotator cuff repair: the effect of double-row fixation on three-dimensional repair site. *J Shoulder Elbow Surg* 2006; **15**: 691-696 [PMID: 17126241 DOI: 10.1016/j.jse.2006.03.004]
- 56 **Rudzki JR**, Shaffer B. New approaches to diagnosis and arthroscopic management of partial-thickness cuff tears. *Clin Sports Med* 2008; **27**: 691-717 [PMID: 19064151 DOI: 10.1016/j.csm.2008.06.004]
- 57 **Dines JS**, Jones K, Maher P, Altchek D. Arthroscopic Management of Full-Thickness Rotator Cuff Tears in Major League Baseball Pitchers: The Lateralized Footprint Repair Technique. *Am J Orthop* (Belle Mead NJ) 2016; **45**: 128-133 [PMID: 26991564]
- 58 **Payne LZ**, Altchek DW, Craig EV, Warren RF. Arthroscopic treatment of partial rotator cuff tears in young athletes. A preliminary report. *Am J Sports Med* 1997; **25**: 299-305 [PMID: 9167807 DOI: 10.1177/036354659702500305]
- 59 **Neri BR**, ElAttrache NS, Owsley KC, Mohr K, Yocum LA. Outcome of type II superior labral anterior posterior repairs in elite overhead athletes: Effect of concomitant partial-thickness rotator cuff tears. *Am J Sports Med* 2011; **39**: 114-120 [PMID: 20940452 DOI: 10.1177/0363546510379971]
- 60 **Andrews JR**, Dugas JR. Diagnosis and treatment of shoulder injuries in the throwing athlete: the role of thermal-assisted capsular shrinkage. *Instr Course Lect* 2001; **50**: 17-21 [PMID: 11372312]
- 61 **Riand N**, Levigne C, Renaud E, Walch G. Results of derotational humeral osteotomy in posterosuperior glenoid impingement. *Am J Sports Med* 1998; **26**: 453-459 [PMID: 9617413]

P- Reviewer: Carbone S, Ertem K, Ko SH, Vulcano E
S- Editor: Ji FF **L- Editor:** A **E- Editor:** Lu YJ



Lessons learned from study of congenital hip disease in adults

George Hartofilakidis, Kalliopi Lampropoulou-Adamidou

George Hartofilakidis, Kalliopi Lampropoulou-Adamidou, Laboratory for the Research of Musculoskeletal System "Th. Garofalidis", Medical School, University of Athens, General Hospital of Athens KAT, Athens 14561, Greece

Author contributions: Professor Hartofilakidis G contributed to the conception of the study; both authors were involved in the design of the study and acquisition of the data, drafting the article and final approval of the version of the article to be published.

Conflict-of-interest statement: The authors declare no conflicts of interest regarding this manuscript.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: George Hartofilakidis, MD, FACS, Professor Emeritus, Laboratory for the Research of Musculoskeletal System "Th. Garofalidis", Medical School, University of Athens, General Hospital of Athens KAT, 10 Athinas Str., Kifissia, Athens 14561, Greece. geo@hart7.com
Telephone: +30-21-03610990

Received: April 14, 2016

Peer-review started: April 18, 2016

First decision: June 14, 2016

Revised: June 29, 2016

Accepted: August 27, 2016

Article in press: August 29, 2016

Published online: December 18, 2016

Abstract

Orthopaedic surgeons specialising in adult hip recon-

struction surgery often face the problem of osteoarthritis secondary to congenital hip disease (CHD). To achieve better communication among physicians, better treatment planning and evaluation of the results of various treatment options, an agreed terminology is needed to describe the entire pathology. Furthermore, a generally accepted classification of the deformities is necessary. Herein, the authors propose the use of the term "congenital hip disease" and its classification as dysplasia, low dislocation and high dislocation. Knowledge of the CHD natural history facilitates comprehension of the potential development and progression of the disease, which differs among the aforementioned types. This can lead to better understanding of the anatomical abnormalities found in the different CHD types and thus facilitate preoperative planning and choice of the most appropriate management for adult patients. The basic principles for improved results of total hip replacement in patients with CHD, especially those with low and high dislocation, are: Wide exposure, restoration of the normal centre of rotation and the use of special techniques and implants for the reconstruction of the acetabulum and femur. Application of these principles during total hip replacement in young female patients born with severe deformities of the hip joint has led to radical improvement of their quality of life.

Key words: Congenital hip disease; Low dislocation of the hip; Hartofilakidis classification; Dysplasia of the hip; High dislocation of the hip; Total hip replacement; Trochanteric osteotomy; Restoration of the normal centre of rotation; Femoral shortening; Patients' satisfaction

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This review is based on the knowledge and experience acquired in the long course of the senior author's surgical practice on the complex problem of congenital deformities of the hip in adults.

Hartofilakidis G, Lampropoulou-Adamidou K. Lessons learned

from study of congenital hip disease in adults. *World J Orthop* 2016; 7(12): 785-792 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/785.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.785>

INTRODUCTION

Congenital deformities of the hip are the main cause of secondary joint osteoarthritis (OA). Depending on the severity of the deformity, undiagnosed patients or those treated insufficiently in infancy face the problem of OA earlier or later in their adult life.

Initially, before the introduction of total hip replacement (THR), we were treating adult patients with different types of osteotomies, without having enough knowledge of the pathological anatomy and the natural history of the underlying deformity. This explains why the results of osteotomies were not always satisfactory. Later, when we started to treat these patients with THR, we realised that the anatomy of the joint differs between patients, thus requiring adjustment of the surgical technique. Since then, the complex problem of congenital hip deformities became one of the main scientific interests of the senior author (GH). Lessons learned, in the long course of this experience, are summarised in this review article.

Lesson 1

The first lesson involves the understanding of the nature of the hip deformities present at birth. The terms used for these deformities were mostly misleading, causing misunderstandings and confusion. We have been concerned about the term "developmental dysplasia of the hip" (DDH) for two reasons: (1) The term "developmental" is not descriptive of the congenital origin of the deformity; and (2) An indiscriminate use of the term "dysplasia" is not in agreement with the variety of the underlying pathology. Therefore, we recommend the use of the term "congenital hip disease" (CHD) for the entire spectrum of related deformities. These deformities are congenital in nature and have the potential to develop.

Furthermore, we recognized that for better communication, planning of treatment and evaluation of the results of different treatments, a classification system of general acceptance must be used. Weinstein had classified CHD in infancy in three radiographic types: (1) dysplasia (inclination of the acetabulum with centralized ossification centre - Shenton's line intact); (2) subluxation (subluxed ossification centre - Shenton's line broken); and (3) complete dislocation (ossification centre outside the acetabulum) (Figure 1). Based on that classification, we identified in adults three different CHD types of increasing severity: (1) dysplasia; (2) low dislocation; and (3) high dislocation. Depending on the type, adjustment of our surgical technique during THR is required. In dysplasia, the femoral head is contained within the original acetabulum.

In low dislocation, the femoral head articulates with a false acetabulum that partially covers the true acetabulum. In high dislocation, the femoral head is migrated superiorly and posteriorly to the hypoplastic true acetabulum. The proximal part of the femur, in dysplasia, is normal. In low dislocation, the femoral neck is short, and shorter still in a high dislocation, with excessive anteversion. The diaphysis, in high dislocation, is hypoplastic with excessive narrowing of the femoral canal and has thin cortices (Figure 2).

Later, in a refinement of our classification system, we further subdivided low and high dislocation. Low dislocation was subdivided into B1 and B2 subtypes, when the false acetabulum covers more or less than 50% of the true acetabulum, respectively. High dislocation was subdivided into C1 and C2 subtypes, depending on the presence or the absence of a false acetabulum, respectively (Figures 3 and 4). The lesson learned by using this classification system is that "better comprehension of the pathologic anatomy and the specific characteristics of these hips, makes their THR reconstruction easier and more successful"^[1-9].

Lesson 2

The second lesson learned is that knowledge of the natural history of CHD facilitates comprehension of the potential development and progression of the disease, which differs among the three types. This can lead to better understanding of the anatomical abnormalities found in the different types, thus facilitating preoperative planning and choice of the most appropriate management for adult patients.

In our country, before the introduction of screening systems, the majority of infant dysplastic hips remained undiagnosed until the onset of symptoms, usually at the third decade of a patient's life. Degenerative changes progress slowly since that time and, usually, THR can be postponed until the age of 45-50 years. Patients with low dislocation, who had not received previous treatment in infancy, limp since childhood and experience pain later in their lives, usually at the age of 25-30 years. In these cases, degenerative changes develop within the false acetabulum and THR, usually becomes necessary earlier than in dysplastic hips. Patients with high dislocation and no previous treatment also limp since early childhood. Limping is more severe in patients with unilateral involvement. Natural history depends on the presence or absence of a false acetabulum. In patients with a false acetabulum pain starts early, usually around 30 years of age, while in patients without a false acetabulum pain starts much later, around the age of 40-45 years, as a consequence of muscle fatigue (Figures 5-7). In unilateral involvement, the leg-length discrepancy ranges between 4-10 cm and increases the disability of the patient. Also, the ipsilateral knee presents valgus deformity, sometimes severe, and the spine thoracolumbar scoliosis.

The indication for a THR not only depends on the degree of pain and disability, but also includes emotional

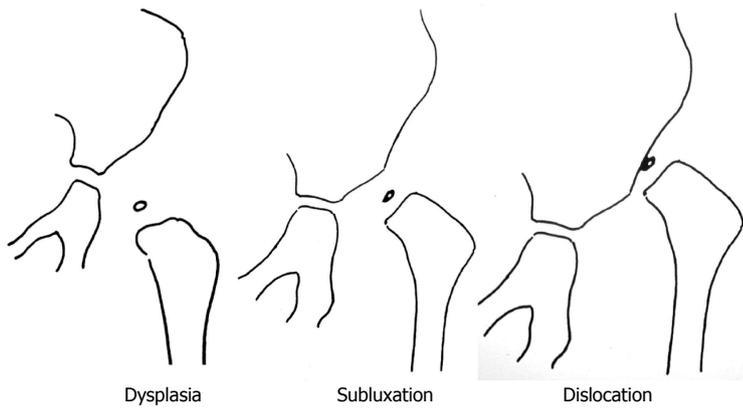


Figure 1 Drawings of the three types of the disease in infants.

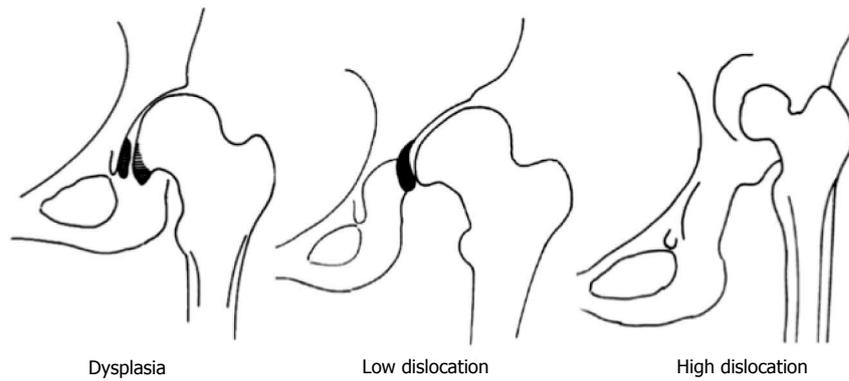


Figure 2 Drawings and three dimensional-computed tomography images of the 3 types of congenital hip disease in adults. The black-colored areas in dysplasia represents the large osteophyte that covers the acetabular fossa and the medial marginal osteophyte of the femoral head (capital drop), and in low dislocation it the inferior part of the false acetabulum that is an osteophyte which begins at the level of the superior rim of the true acetabulum.



parameters, given that these patients are young females with an active and productive life^[10,11].

Lesson 3

Another lesson learned is that THR is a difficult operation and should be performed by experienced surgeons and only when there is an absolute indication based on the patient's symptoms, psychological impact, clinical findings and the potential of disease development; "Not to early, not to late". Several technical details should be considered^[9,12-17].

Transtrochanteric approach: Wide exposure is essential for the reconstruction, especially of hips with low and high dislocation. The lateral transtrochanteric approach was introduced by Charnley, who suggested that it would facilitate the access to the joint and the reconstruction of the disturbed anatomy of the acetabulum and the proximal femur. Additionally, lateral reattachment of the trochanter increases the abductor lever arm and

minimises the reactive forces acting on the acetabulum. Four categories of the trochanteric reattachment are recognised: (1) reattachment at the original bed of trochanteric osteotomy; (2) distal reattachment in relation to its original bed, the trochanter having contact with the distal part of the original bed; (3) reattachment on the lateral femoral cortex in cases where the femoral neck was resected to the level of the lesser trochanter; and (4) reattachment proximal to its original bed (Figure 8). The ideal reattachment of the trochanter is the distal reattachment retaining contact with the distal part of the original bed. However, this is not always possible mainly due to shortened abductor muscles, an often small and malpositioned trochanter and a lengthened limb^[16].

The most common complication of trochanteric osteotomy is the non-union of the trochanteric fragment. Other complications include breakage and migration of the wires, heterotopic ossification and dislocation. We learned that the complications of this exposure were less

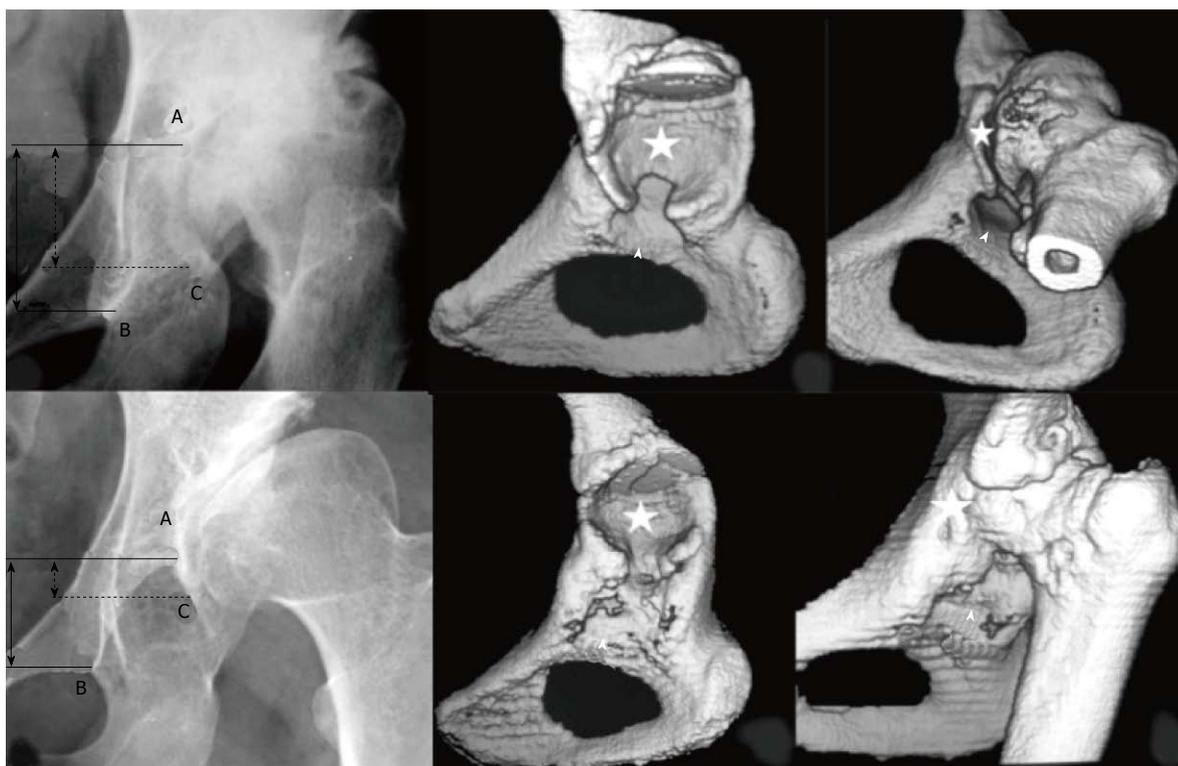


Figure 3 Images illustrating the two subtypes of low dislocation: B1 and B2. Three points must be recognised on radiographs: (A) the superior limit of the true acetabulum; (B) the inferior point of the teardrop; (C) the most inferior point of the false acetabulum. Three dimensional-computed tomography scans may help to determine the superior limit of the true acetabulum, when it is not clear in plain radiographs. Asterisks depict false acetabulum and arrowheads true acetabulum.

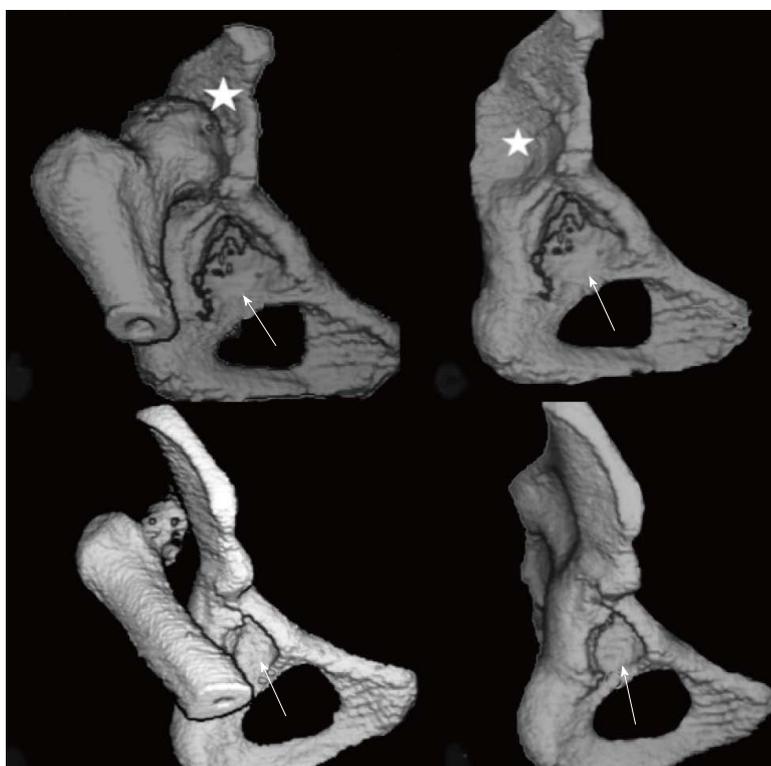


Figure 4 Three dimensional-computed tomography scans of the two subtypes of high dislocation. Arrows indicate the true and asterisks the false acetabulum.

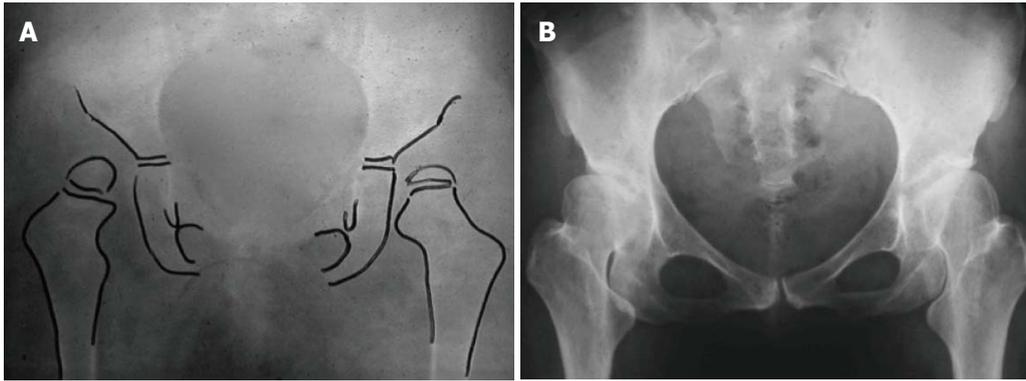


Figure 5 Development of dysplastic hips. A: At the age of 3 years, when the child was first seen by her physician. An abduction frame was applied for 6 mo; B: At the age of 35 years, the patient had the first symptoms, pain and limping, due to the development of secondary hip osteoarthritis.

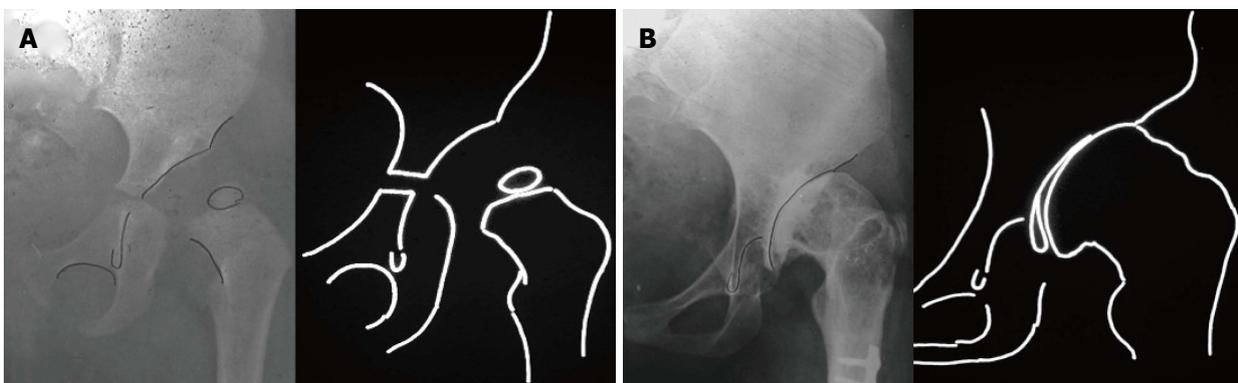


Figure 6 Radiographs and diagrams of a female patient with subluxation of the left hip in infancy, subsequently developed to low dislocation. A: At the age of 2 years; B: Image, when the patient was 37 years old.

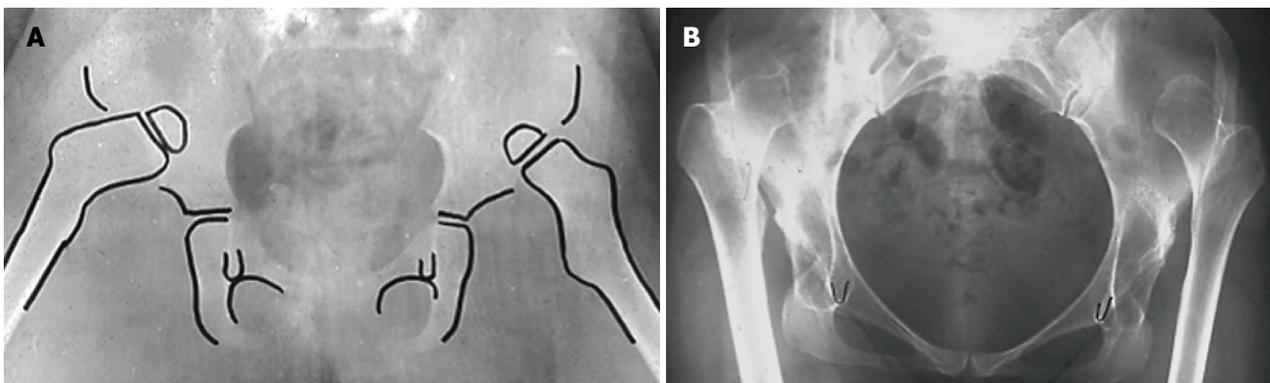


Figure 7 Images illustrating the case of a female patient with bilateral high dislocation. A: Radiograph at the age of 2 years; B: Radiograph, at the age of 33 years, when the patient was consulted for bilateral total hip replacements.

important than the benefits gained^[16].

Restoration of the normal centre of rotation of the joint: Placement of the acetabular component at the level of true acetabulum is essential for restoration of the hip biomechanics and improvement of survival of the prosthesis. However, it is not always possible to achieve bony coverage of the acetabular component at this level. Two alternative techniques have been used to solve this problem. When the reamed acetabulum

can provide at least 80% osseous coverage of the implant, we use an uncemented small 40-42 mm metal backed acetabular component. If this is not feasible, the cotyloplasty technique is an effective alternative. Cotyloplasty involves medialization of the acetabular floor through creation of a comminuted fracture of the entire medial wall, impaction of autogenous cancellous morselized bone grafts and implantation of a small, all-polyethylene (PE) implant, usually the offset-bore acetabular cup (Figure 9)^[3,9,14]. The main mechanical

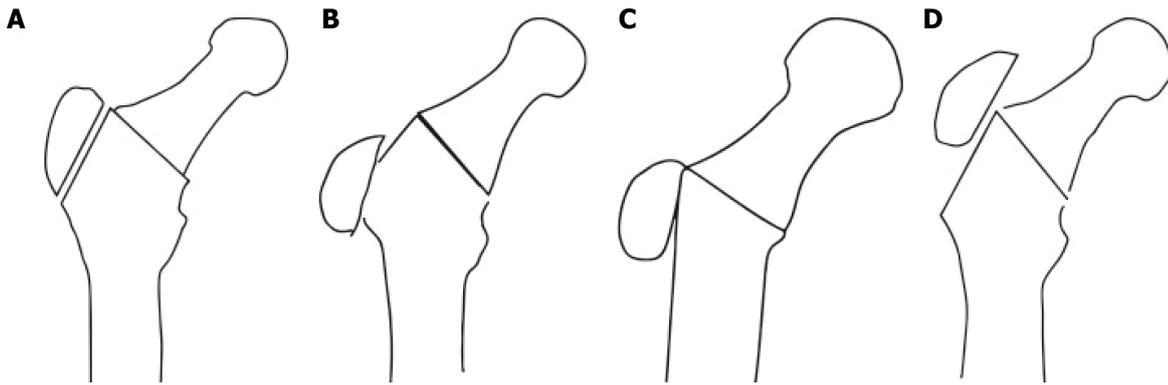


Figure 8 Drawings depicting. A: Reattachment of the trochanter at its original bed; B: Distal reattachment of the trochanter, retaining contact with the distal part of the original bed; C: Reattachment of the trochanter on the lateral femoral cortex; D: Proximal reattachment of the trochanter.

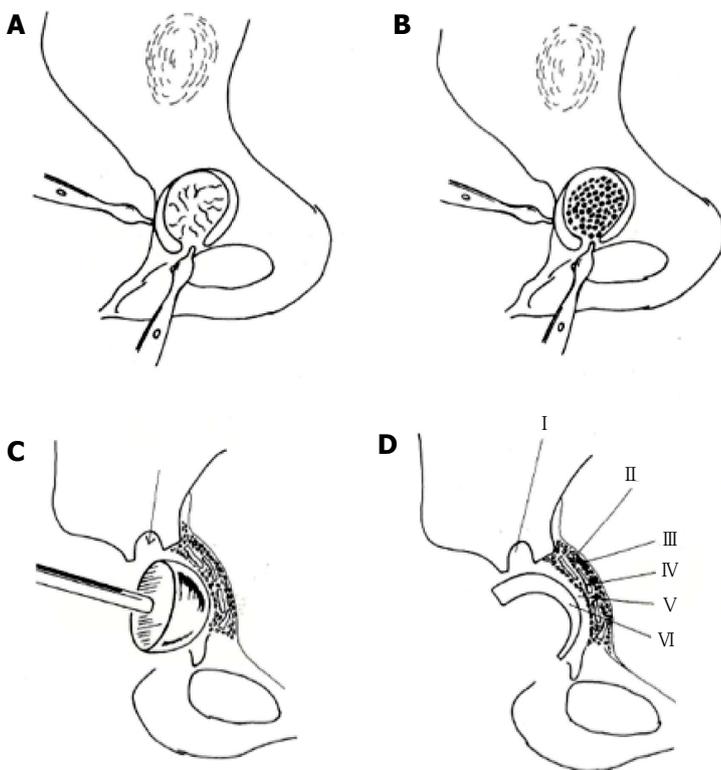


Figure 9 Cotyloplasty technique. A: Comminuted fracture of the entire medial wall; B: Large amount of cancellous morselised graft placed between the fragments of the acetabular floor, onto the periosteum; C: Grafts moulded with a hemispherical pusher; D: Final appearance: I: Anchorage hole; II: Internal layer of the periosteum; III: Autogenous morselised graft; IV: Fragments of the acetabular floor; V: Cement mantle; VI: Offset-bore acetabular component.

advantage of this technique is that the weight-bearing area is allowed to shift to beneath the acetabular roof, while adequate anterior and posterior coverage of the cup is achieved. Moreover, the host-graft interface is biologically active, which may ensure incorporation of the graft and the anatomical placement of the cup. This, combined with carefully controlled medialization optimizes the mechanical environment and influences the long-term survival of the artificial hip.

On the other hand, augmentation of superior segmental defects with structural autograft or allograft and placement of the acetabular component in the anatomical position had been suggested by Harris *et al.*^[18]. Although the short-term results of this technique were excellent, a high failure rate after approximately 12 years has been reported^[19]. This may be related

to the complex pathological anatomy encountered at the level of the true acetabulum and the abnormal distribution of stresses, combined with the unfavourable long-term biological behaviour of structural grafts^[3,9].

Shortening of the femur: For hips with high dislocation, shortening of the femur during THR is inevitable. We favour shortening of the femur by progressive resection of bone at the level of the femoral neck. We argue against leaving the greater trochanter in place and subtrochanteric femoral shortening osteotomy, because, in the majority of hips with high dislocation, the greater trochanter lies above the centre of rotation of the femoral head and its resection and advancement are essential (Figure 10). Besides, subtrochanteric osteotomy resembles an artificial fracture which needs additional osteosynthesis and may

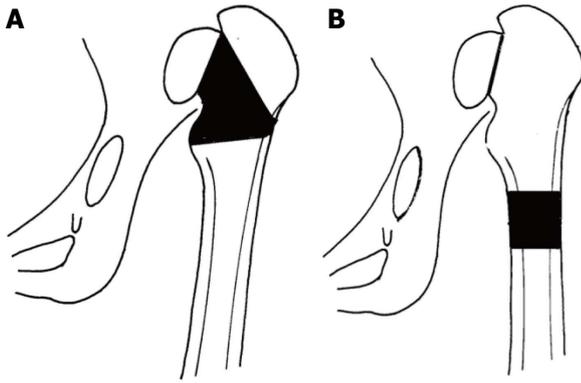


Figure 10 Drawings of the two alternatives of shortening of the femur. A: At the level of femoral neck; B: Distal shortening at the level of femoral shaft.

subsequently cause undesirable complications^[9].

Special implants: Special small implants are needed. We have been using the Chamley's offset bore cup in most of our cases. It is an extra small all-PE implant with a 35 mm face diameter, offset articular surface and approximately 10 mm PE thickness at the upper weight-bearing part, equal to that of a conventional socket, that decreases to a few millimetres in the lower part. In cases with a narrow femoral canal and short and anteverted neck, for the reconstruction of the femur we have mostly used the stainless steel Chamley CDH stems with polished surface, monoblock and collarless, and the Harris CDH stem made of CoCr, precoated at the proximal part, modular and with collar^[20-22]. Currently new cementless designs are used.

Lesson 4

Females with congenital dislocation of the hip represent a special cohort of patients with a problematic life since birth. These patients are of young age and may have pain, severe limping and deformation, major leg-length discrepancies and several psychological disorders, such as anxiety and depression, since their early childhood. We evaluated the quality of life (QoL) of 82 female patients, with low and high dislocation, followed for a minimum of 12 years after THR using clinical scores and QoL questionnaires. We concluded that THR radically improves their QoL for a long period of time. Even patients who subsequently underwent revisions had enjoyed pain relief and functional improvement for an appreciable period of time^[23].

Letters from these patients, many years after surgery, show their satisfaction for the great changes in their physical and psychological status as well as their social and family life. Short excerpts from this communication are the following^[24]: "My childhood was a life of torment. My mother used to tell me that no man is going to love me. She made me feel useless. My life changed after surgeries at the age of 28. I got married and now I have a 15-year-old son. We are a happy family"; "My childhood and teenage life were very difficult, with many complexities

and insecurities. I was feeling like a child of an inferior God. I took the decision to have an arthroplasty at the age of 29. Even though it was necessary to be operated again after 11 years, I am now fully active leading a normal life. I am very pleased"; "My life was an Odyssey. At school, the children were making fun of me for being so different to them because of my pelvic deformity and my movements. When I had the arthroplasties in my hips, I was 47 years old. My life changed. I look at the mirror and I do not believe my eyes. People who knew me did not recognize me. Twenty-four years have gone since I was operated and I have a normal life".

Concluding messages

The most suitable term for the total spectrum of congenital hip deformities is "CHD", classified in adults into dysplasia (type A), low dislocation (type B) and high dislocation (type C). Types B and C are further subdivided in subtypes B1 and B2, and C1 and C2, respectively, depending on their different anatomic characteristics.

The three types of CHD are the main causes of secondary OA. Degenerative changes develop gradually, usually from the age of 30-35 years, causing pain and increasing functional disability over time. Knowledge of the natural history of the three types of CHD facilitates choosing the most appropriate time for THR.

The transtrochanteric approach is essential in cases with low and high dislocation and in certain dysplastic hips with great limitation of the range of motion.

Restoration of the normal centre of rotation is fundamental for the joint biomechanics and the survival of the prosthesis.

Shortening of the femur, if needed, is better to be performed at the level of the femoral neck.

In the majority of cases, special implants are needed to reconstruct the acetabulum and the femur.

The improvement of the QoL, especially in young females with high dislocation, is impressive. Most of these patients stated that after surgery they feel "like they were born gain".

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Konstantina Stathopoulou for her kind suggestions regarding the writing style of this work.

REFERENCES

- 1 **Hartofilakidis G**, Babis GC, Lampropoulou-Adamidou K. Congenital Hip Disease: General Aspects, Terminology and Classification. In: Congenital Hip Disease in Adults. Italy: Springer-Verlag Italia, 2014: 11-27
- 2 **Hartofilakidis G**, Stamos K, Ioannidis TT. Low friction arthroplasty for old untreated congenital dislocation of the hip. *J Bone Joint Surg Br* 1988; **70**: 182-186 [PMID: 3346284]
- 3 **Hartofilakidis G**, Stamos K, Karachalios T, Ioannidis TT, Zacharakis N. Congenital hip disease in adults. Classification of acetabular deficiencies and operative treatment with acetabuloplasty combined

- with total hip arthroplasty. *J Bone Joint Surg Am* 1996; **78**: 683-692 [PMID: 8642024]
- 4 **Hartofilakidis G.** Developmental dysplasia of the hip: An unsuitable term. *J Bone Joint Surg Am* 2004; **86-A**(2)
 - 5 **Yiannakopoulos CK, Xenakis T, Karachalios T, Babis GC, Hartofilakidis G.** Reliability and validity of the Hartofilakidis classification system of congenital hip disease in adults. *Int Orthop* 2009; **33**: 353-358 [PMID: 17985130 DOI: 10.1007/s00264-007-0472-0]
 - 6 **Yiannakopoulos CK, Chougle A, Eskelinen A, Hodgkinson JP, Hartofilakidis G.** Inter- and intra-observer variability of the Crowe and Hartofilakidis classification systems for congenital hip disease in adults. *J Bone Joint Surg Br* 2008; **90**: 579-583 [PMID: 18450622 DOI: 10.1302/0301-620X.90B5.19724]
 - 7 **Hartofilakidis G, Yiannakopoulos CK, Babis GC.** The morphologic variations of low and high hip dislocation. *Clin Orthop Relat Res* 2008; **466**: 820-824 [PMID: 18288552 DOI: 10.1007/s11999-008-0131-9]
 - 8 **Hartofilakidis G, Babis GC.** Congenital disease of the hip. *Clin Orthop Relat Res* 2009; **467**: 578-579 [PMID: 19030940 DOI: 10.1007/s11999-008-0629-1]
 - 9 **Karachalios T, Hartofilakidis G.** Congenital hip disease in adults: terminology, classification, pre-operative planning and management. *J Bone Joint Surg Br* 2010; **92**: 914-921 [PMID: 20595107 DOI: 10.1302/0301-620X.92B7.24114]
 - 10 **Hartofilakidis G, Babis GC, Lampropoulou-Adamidou K.** Epidemiology, Demographics and Natural History. In: *Congenital Hip Disease in Adults*. Italy: Springer-Verlag Italia, 2014: 29-43
 - 11 **Hartofilakidis G, Karachalios T, Stamos KG.** Epidemiology, demographics, and natural history of congenital hip disease in adults. *Orthopedics* 2000; **23**: 823-827 [PMID: 10952045]
 - 12 **Hartofilakidis G, Babis GC, Lampropoulou-Adamidou K.** Technical Considerations. In: *Congenital Hip Disease in Adults*. Italy: Springer-Verlag Italia, 2014: 63-75
 - 13 **Stamos KG, Karachalios T, Papagelopoulos PJ, Xenakis T, Korres DS, Koroneos E, Hartofilakidis G.** Long-term mechanical stability of the impacted morselized graft-cement interface in total joint replacement: an experimental study in dogs. *Orthopedics* 2000; **23**: 809-814 [PMID: 10952043]
 - 14 **Hartofilakidis G, Stamos K, Karachalios T.** Treatment of high dislocation of the hip in adults with total hip arthroplasty. Operative technique and long-term clinical results. *J Bone Joint Surg Am* 1998; **80**: 510-517 [PMID: 9563380]
 - 15 **Hartofilakidis G, Karachalios T.** Total hip arthroplasty for congenital hip disease. *J Bone Joint Surg Am* 2004; **86-A**: 242-250 [PMID: 14960667]
 - 16 **Hartofilakidis G, Babis GC, Georgiades G, Kourlaba G.** Trochanteric osteotomy in total hip replacement for congenital hip disease. *J Bone Joint Surg Br* 2011; **93**: 601-607 [PMID: 21511924 DOI: 10.1302/0301-620X.93B5.24780]
 - 17 **Hartofilakidis G, Karachalios T, Georgiades G, Kourlaba G.** Total hip arthroplasty in patients with high dislocation: a concise follow-up, at a minimum of fifteen years, of previous reports. *J Bone Joint Surg Am* 2011; **93**: 1614-1618 [PMID: 21915576 DOI: 10.2106/JBJS.J.00875]
 - 18 **Harris WH, Crothers O, Oh I.** Total hip replacement and femoral-head bone-grafting for severe acetabular deficiency in adults. *J Bone Joint Surg Am* 1977; **59**: 752-759 [PMID: 908698]
 - 19 **Mulroy RD, Harris WH.** Failure of acetabular autogenous grafts in total hip arthroplasty. Increasing incidence: a follow-up note. *J Bone Joint Surg Am* 1990; **72**: 1536-1540 [PMID: 2254363]
 - 20 **Ioannidis TT, Zacharakis N, Magnissalis EA, Eliades G, Hartofilakidis G.** Long-term behaviour of the Charnley offset-bore acetabular cup. *J Bone Joint Surg Br* 1998; **80**: 48-53 [PMID: 9460952 DOI: 10.1302/0301-620X.80B1.8057]
 - 21 **Hartofilakidis G, Georgiades G, Babis GC, Yiannakopoulos CK.** Evaluation of two surgical techniques for acetabular reconstruction in total hip replacement for congenital hip disease: results after a minimum ten-year follow-up. *J Bone Joint Surg Br* 2008; **90**: 724-730 [PMID: 18539664 DOI: 10.1302/0301-620X.90B6.20490]
 - 22 **Digas G, Georgiades G, Lampropoulou-Adamidou K, Hartofilakidis G.** The twenty-year survivorship of two CDH stems with different design features. *Eur J Orthop Surg Traumatol* 2013; **23**: 901-906 [PMID: 23412232 DOI: 10.1007/s00590-012-1105-x]
 - 23 **Roidis NT, Pollalis AP, Hartofilakidis GC.** Total hip arthroplasty in young females with congenital dislocation of the hip, radically improves their long-term quality of life. *J Arthroplasty* 2013; **28**: 1206-1211 [PMID: 23566699 DOI: 10.1016/j.arth.2012.09.025]
 - 24 **Hartofilakidis G, Babis GC, Lampropoulou-Adamidou K.** Quality of Life After Total Hip Replacement. In: *Congenital Hip Disease in Adults*. Italy: Springer-Verlag Italia, 2014: 131-163

P- Reviewer: Fukiage K, Macheras GA, Zahar A **S- Editor:** Qiu S
L- Editor: Wang TQ **E- Editor:** Lu YJ



Fifth metatarsal fractures and current treatment

Julia Bowes, Richard Buckley

Julia Bowes, Department of Surgery, Division of Orthopedics, Walter Mackenzie Centre, University of Alberta, Edmonton, AB T6G 2B7, Canada

Richard Buckley, Department of Surgery, Section of Orthopedics, Foothills Medical Centre, University of Calgary, Calgary, AB T2N 5A1, Canada

Author contributions: Bowes J performed the majority of the writing; Buckley R designed the manuscript outline, contributed to the writing and performed the majority of the editing.

Conflict-of-interest statement: The authors have no conflict of interests to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Julia Bowes, MD, Department of Surgery, Division of Orthopedics, Walter Mackenzie Centre, University of Alberta, 8440 112 Street NW, Edmonton, AB T6G 2B7, Canada. jbowes@ualberta.ca
Telephone: +1-587-9897970

Received: June 27, 2016

Peer-review started: June 29, 2016

First decision: August 5, 2016

Revised: September 15, 2016

Accepted: October 5, 2016

Article in press: October 7, 2016

Published online: December 18, 2016

Abstract

Metatarsal fractures are one of the most common injuries of the foot. There has been conflicting literature

on management of fifth metatarsal fractures due to inconsistency with respect to classification of these fractures. This article provides a thorough review of fifth metatarsal fractures with examination of relevant literature to describe the management of fifth metatarsal fractures especially the proximal fracture. A description of nonoperative and operative management for fifth metatarsal fractures according to anatomical region is provided.

Key words: Metatarsal fractures; Fifth metatarsal; Jones fracture; Operative care; Athlete

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Nondisplaced fifth metatarsal fractures can be treated nonoperatively depending on fracture location and patient factors. When nonoperative management is utilized improved early functional scores are associated with less rigid immobilization and a shorter period of nonweightbearing. Neck and shaft fractures with greater than ten degrees plantar angulation or three millimeters of displacement in any plane where closed reduction is insufficient require operative management. Operative intervention is recommended for base of the fifth metatarsal avulsion fractures (zone one) with more than three millimeters of displacement. Acute and delayed union zone two fractures may be managed nonoperatively but operative management with an intramedullary screw should be considered in athletes. Zone three (diaphyseal stress fractures) fractures that are Torg type I and type II should be managed with intramedullary screw fixation in the athlete. In the non-athlete these fractures may be managed nonoperatively however prolonged immobilization is often required and a nonunion may still result. Symptomatic nonunions of zone two and zone three fractures should be managed operatively.

Bowes J, Buckley R. Fifth metatarsal fractures and current treatment. *World J Orthop* 2016; 7(12): 793-800 Available from: <http://www.wjgnet.com/2218-5836/full/v7/i12/793.htm>

INTRODUCTION

Metatarsal fractures are frequently encountered injuries of the foot^[1]. Approximately five to six percent of fractures encountered in the primary care setting are metatarsal fractures^[2]. In adults, metatarsal fractures peak in the second to fifth decades of life. The most frequent fracture seen is the fifth metatarsal, accounting for 68% of metatarsal fractures^[2]. Proximal fifth metatarsal fractures are divided into three zones^[3-5]. Zone one, zone two, and zone three fractures account for 93%, four percent and three percent of proximal fifth metatarsal fractures, respectively^[6]. There is some evidence-based literature to help make decisions with these fracture types, which will be described in this review.

CLASSIFICATION

The first to describe a fracture of the proximal fifth metatarsal was Sir Robert Jones^[7-9]. He described a fracture in the proximal three quarter segment of the shaft distal to the styloid^[7-9]. The Jones fracture as described by Sir Robert Jones was later defined by Stewart^[10,11] as a transverse fracture at the junction of the diaphysis and metaphysis without extension into the fourth and fifth intermetatarsal articulation. Since then there has been a focus in the literature on fractures of the proximal fifth metatarsal due to the propensity for poor healing of some fractures in this region. The blood supply to the proximal fifth metatarsal is important in understanding troublesome fracture healing in this area. The blood supply of the fifth metatarsal was investigated in a cadaver model by Smith *et al.*^[12]. They found that the blood supply arises from three possible sources; the nutrient artery, the metaphyseal perforators, and the periosteal arteries. A watershed area exists between the supply of the nutrient artery and the metaphyseal perforators which corresponds to the area of poor fracture healing in the clinical setting^[12]. A classification system created by Torg *et al.*^[13] is based on healing potential. This classification simplifies proximal fifth metatarsal fractures as either involving the tuberosity or the proximal diaphysis distal to the tuberosity, the latter group being called the Jones fracture^[13,14]. Under this system the Jones fracture is divided into three types based on the radiological appearance of the fracture^[13]. Type I (acute) fractures are characterized by a narrow fracture line and an absence of intramedullary sclerosis^[13,15,16]. The features of acute fractures in this classification are no history of previous fracture, although previous pain or discomfort may be present^[13]. Torg type I fractures are presumed to be acute fractures at a site of pre-existing stress concentration on the lateral cortex that becomes acutely disabling when they extend across the entire diaphysis^[13].



Figure 1 Radiograph of a Torg type II fifth metatarsal fracture.



Figure 2 Radiograph of a fifth metatarsal Torg type III fracture, which has nonunited.

Type II (delayed union) are distinguished by having a previous injury or fracture with radiographic features of a widened fracture line and evidence of intramedullary sclerosis (Figure 1)^[13,15,16]. Type III (nonunion) are characterized by complete obliteration of the medullary canal by sclerotic bone with a history of repetitive trauma and recurrent symptoms (Figure 2)^[13,15,16]. Although the term Jones fracture was applied to the fractures in this classification, based on Torg's description these fractures are more consistent with stress fractures. As a result, proximal fifth metatarsal fractures were re-classified to avoid the confusing term of Jones fractures. Proximal fifth metatarsal fractures can be classified into three zones as described by Lawrence *et al.*^[3] and Dameron^[4,5]. Tuberosity avulsion fractures represent zone one (Figure 3)^[3-5]. Zone two (Jones fracture) is described as a fracture at the metaphysis-diaphyseal junction. Zone three or diaphyseal stress fractures include the proximal 1.5 cm of the diaphysis^[3,4,5,9,17]. This classification is straightforward however, it must be noted that their description of zone two is a slight mis-representation of the true Jones fracture as described by Stewart^[11]. It is important to note that the Jones fracture in this classification system is an acute injury with no prodrome whereas zone three fractures have a variable prodrome^[3]. The distinction between Jones (zone two) and proximal diaphyseal stress fractures



Figure 3 Radiograph of a zone one fifth metatarsal fracture.

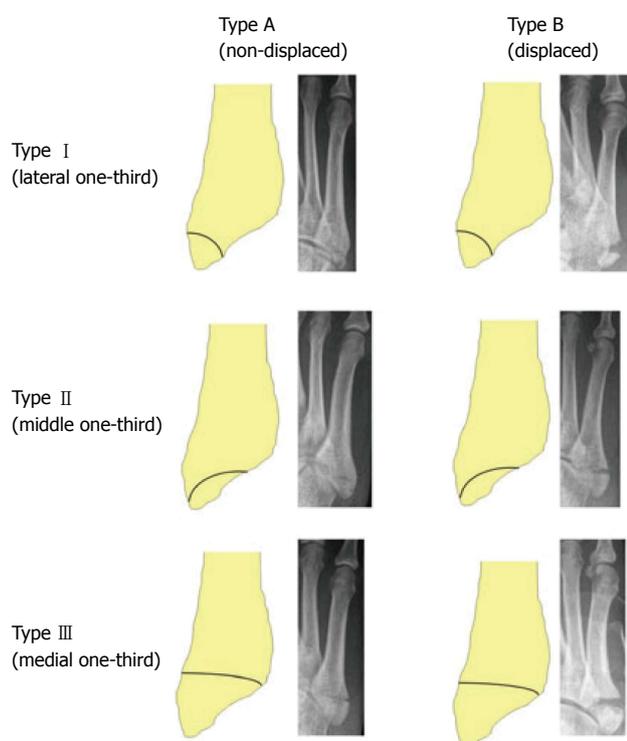


Figure 4 Classification system created by Mehlhorn *et al*^[18] based on risk of displacement with more medial joint entry of the fracture line. Type I, type II, type III are defined as fracture line entry in the lateral one-third, middle one-third and medial one-third, respectively^[18].

(zone three) is commonly confused in the literature which potentially obscures important differences in prognosis and treatment^[3,4,10,15]. A systematic review done by Dean *et al*^[14], looked at the classification of Jones fractures in 19 studies. They found that the majority of authors did not differentiate between fractures involving the fourth/fifth intermetatarsal articulation from more distal fractures. They concluded that the Jones fracture is generally applied to all fractures of the proximal fifth metatarsal distal to the tuberosity within 1.5 cm of this region. However, because this is not a universal definition it very difficult to recognize differences in outcomes between operative and nonoperative management of zone two and zone three fractures in the literature. It also indicates that in many cases the literature fails to differentiate the chronicity of

zone two and zone three fractures^[14].

More recently, Mehlhorn *et al*^[18] proposed another classification for base of fifth metatarsal fractures based on radiomorphometric analysis reflecting the risk for secondary displacement. In this classification the joint surface of the fifth metatarsal base is divided into three equal parts. Type I, type II, and type III fractures represent the lateral third, middle third, and medial third respectively (Figure 4). Adding to this classification they introduced an A type which represents no relevant displacement and a B type which denotes a fracture step off of greater or equal to two millimetres^[18].

CLINICAL PRESENTATION AND ASSESSMENT

An injury to the fifth metatarsal presents with history of acute trauma or repetitive trauma to the forefoot^[19]. Zone one fractures are typically avulsion type injuries. The mechanism of these fractures are an acute episode of forefoot supination with plantar flexion^[3,19,20]. This results in pull from the lateral band of the plantar fascia and peroneus brevis^[20]. Typically, the fracture pattern is transverse to slightly oblique. Occasionally, these fractures are comminuted, significantly displaced or disrupt the cuboid-base of fifth metatarsal joint^[6]. Zone two fractures result from an acute episode^[3-5]. The exact mechanism is not known but is thought to result from a large adduction force applied to the forefoot with the ankle plantar flexed^[3,4,19]. Zone three fractures (diaphyseal stress fractures) typically results from a fatigue or stress mechanism^[3]. Stress fractures of the proximal fifth metatarsal have been defined by DeLee *et al*^[1] as a spontaneous fracture of normal bone that results from a summation of stresses any of which by itself would be harmless. Multiple factors contribute to the development of stress fractures including systemic factors, anatomic factors, and mechanical factors^[1]. Although multiple factors contribute the exact mechanical mechanism is unclear. It is thought that either muscle creates a localized force that outweigh the stress-bearing capacity of bone or that when muscle fatigues excessive forces are transmitted to the surrounding bone^[19].

Radiographic imaging for a suspected metatarsal fracture includes three standard radiographic views of the foot: Lateral, anteroposterior, and a 45 degree oblique. Acute stress fractures are typically not detected on the standard three views of the foot. It is suggested that repeated radiographs are made at 10 to 14 d after the initial onset of symptoms^[9]. At this time a radiolucent reabsorption gap around the fracture confirms the diagnosis^[9]. In the case of more complex midfoot trauma, a CT scan is recommended to rule out the Lisfranc fracture dislocation^[9].

INDICATION FOR SURGERY

Management of fifth metatarsal fractures depends on the classification of the fracture, the nature of other



Figure 5 Radiograph showing healing in a nonunion treated with a percutaneous 3.5-mm cortical lag screw.

injuries sustained, and patient demographics. Taking everything into consideration, along with patient activity level, treatment can be nonoperative or operative.

If there is more than three to four millimeters displacement or ten degrees of plantar angulation of neck or shaft fractures and closed reduction is not sufficient, operative intervention is recommended^[10].

Avulsion fractures of the base of the fifth metatarsal that are displaced greater than three millimetres or comminuted should be reduced and operatively fixed^[7]. Fracture reduction and fixation should be considered if the fracture fragment involves more than 30% of the cubometatarsal joint^[10]. Mehlhorn *et al*^[18] recommended (based on their radiomorphometric analysis) that fractures with larger than a two millimeter step off involving the joint surface be fixed with open reduction internal fixation given the risk for posttraumatic osteoarthritis. They found that fractures they classified as type III A (medial joint fracture) had a 45% risk of secondary displacement. Therefore, they recommend that for these fractures, open reduction and internal fixation be a consideration.

Displaced zone two fractures require operative management. Less consensus exists on acute nondisplaced Jones fractures (zone two). There are many studies that advocate for early intramedullary screw fixation for acute Jones fractures in the active population^[21-24]. Porter *et al*^[21] demonstrated that acute Jones fractures treated operatively resulted in quicker return to sport and clinical healing in competitive athletes. In this same study, athletes returned to sports at a mean of 7.5 wk (range 10 d to 12 wk). This time period is shorter than the average time to healing with nonoperative management. Mindrebo *et al*^[22] described nine athletes that underwent early percutaneous intramedullary screw fixation and the patients were full weightbearing within seven to ten days. They found that on average the patients were able to return to full sport by 8.5 wk and all had radiographic union by an average of six weeks^[22]. Literature published by Quill^[23] reports that one in three nonoperatively treated Jones fractures re-fractured and therefore recommended early surgical management.

Another study by Mologne *et al*^[24] compared non-

operative management with a nonweightbearing cast or early intramedullary screw fixation and weightbearing within 14 d. The operative treatment group demonstrated a reduced time to return to sport and faster clinical union by almost 50% compared to the nonoperative group^[24]. The incidence of treatment failure in the cast treatment group was 44%. However, it should be noted that in this study a Jones fracture was defined as a type I Torg fracture and did not account for the difference between zone two and three fractures^[24].

Zone two delayed unions are a relative indication for surgical intervention. While delayed unions may eventually heal the detrimental effects of prolonged immobilization and nonweightbearing is a reason to consider operative intervention^[3].

Surgical intervention is typically recommended for type II and type III diaphyseal stress fractures, as seen in Figure 5^[4,25]. Delayed unions may eventually heal by nonoperative means but often require prolonged immobilization and nonweightbearing which is a reason to consider operative management^[3,25]. In highly active individuals with a type II diaphyseal stress fracture, operative management is recommended^[3,10,25].

Additionally, when making decision between operative and nonoperative management of zone two and zone three fractures hindfoot varus should be excluded. Evidence of hindfoot varus is thought to be a predisposing factor for these fractures as well as re-fracture following fixation. In one study done by Raikin *et al*^[26], 90% of patients with Jones fractures had evidence of hindfoot varus, whereas the incidence of hindfoot varus in the normal population is approximately 24%. In this study Jones fractures included acute and stress fractures of zone two and zone three. It can be concluded that patients presenting with zone two and zone three fractures and clinical hindfoot varus require correction of the varus to prevent re-fracture after operative or nonoperative management. Raikin *et al*^[26] corrected hindfoot varus with a lateral heel wedge and forefoot post inserts which resulted in no re-fractures of operatively managed fractures.

NONOPERATIVE TREATMENT

There are a number of nonoperative treatment modalities used for metatarsal fractures. They vary by anatomical region, patient history and radiological findings but evidence based medicine has helped with this treatment type. Isolated nondisplaced shaft and neck fractures of the fifth metatarsal are treated nonoperatively^[10,27]. A variety of nonoperative modalities include elastic dressing and a rigid shoe, short leg walking cast, posterior splint, or a hard plastic cast shoe with weightbearing as tolerated^[26]. A study done by O'Malley *et al*^[28] demonstrated that active individuals do well when treated nonoperatively. The study looked at 35 ballet dancers with distal shaft fractures treated nonoperatively and 31 of the patients returned to dance without limitations or pain^[28].

Table 1 Studies comparing nonoperative management of zone 1 proximal fifth metatarsal fractures

Ref.	Treatment modality	Outcome
Shahid <i>et al</i> ^[29]	Airboot compared to below knee walking cast	Pain and function recovered quicker with airboot No difference in time to union between groups
Clapper <i>et al</i> ^[30] Gray <i>et al</i> ^[31]	Hard-soled shoe compared to below knee cast Plastic slipper compared to tubi-grip support	No difference between clinical healing results Fractures treated with a plaster slipper resulted in significantly better pain and function at 2 wk At 6 and 12 wk the outcomes were similar for both treatment groups
Wiener <i>et al</i> ^[32]	Below knee casting compared to soft "Jones" dressings	The average time to union was 33 d vs 46 d respectively for soft dressings compared to rigid casting

Evidence based studies suggest that nondisplaced zone one fractures at the base of the fifth metatarsal are treated with protected weightbearing utilizing one of the many modalities varying from a short leg cast to elastic dressing and rigid shoe only as seen in Table 1^[3,9,26,29-32]. The outcomes of nonoperative treatment for nondisplaced zone one fractures are good with low nonunion rates reported between 0.5% and 1%^[33].

Acute zone two fractures are managed with non-weightbearing in a short leg cast for 6 to 8 wk. Torg type I diaphyseal stress fractures (zone three) are also managed the same however, prolonged immobilization up to twenty weeks may be required^[3,10,13,31]. Despite prolonged immobilization zone three diaphyseal stress fractures may still go on to nonunion. Delayed unions of zone two and type II zone three fractures may eventually heal by nonoperative treatment but operative management is recommended in highly active patient populations^[3,10,13,25]. Additionally, despite prolonged immobilization in zone three fractures it is not uncommon for a nonunion to occur^[3].

There is a clear lack of randomized controlled trials comparing various nonoperative treatment modalities. As a result, the choice of nonoperative management should be based on the patient and the individual fracture type. A retrospective study done by Konkel *et al*^[33], demonstrates the results obtained from nonoperative management of fifth metatarsal fractures. They found that the average time to bony union for tuberosity fractures, Jones, stress, segmental shaft, and oblique distal shaft/neck fractures was 3.7, 3.5, 4.8, 3.6 and 3.4 mo respectively. There was only one nonunion out of the 66 metatarsal fractures, which was a tuberosity fracture. There was delayed union in ten tuberosity fractures, two Jones fractures, two stress fractures and four oblique distal shaft/neck fractures. Overall they found that delayed union was seen in 27% of the patients with an overall union rate of 98.5%. The long-term satisfaction rate with nonoperative management was 100% in 40 patients with long-term follow-up^[33].

One consideration is patients factors associated with less favourable outcomes. Female gender, diabetes mellitus and obesity are associated with adverse outcomes of metatarsal fractures^[34]. One prospective cohort study showed that Torg type III fractures, displacement, and weight were significant independent predictors of poor

outcomes at six weeks^[35]. Additionally, this study showed that at 20 wk in addition to the above factors gender and diabetes were also significant independent predictors of poor outcome^[35].

OPERATIVE TREATMENT

There are a variety of modalities for operative management of proximal fifth metatarsal fractures including percutaneous fixation with an intramedullary screw, corticocancellous bone graft, closed reduction and cross-pinning with Kirschner-wire (K-wire) fixation, or open reduction and internal fixation with minifragment plate and screws^[3,4,9].

Zone one fractures that require operative fixation based on the indications specified in a previous section can be fixed using K-wires, tension band wiring, or small ASIF screws. If an avulsed fragment is too small for fixation excision may be required if chronic irritation results^[3,4,19].

Percutaneous fixation with an intramedullary screw has become the preferred treatment choice for zone two and three fractures requiring operative fixation as specified in the indications for surgery section^[3,15,19,24,25]. The advantage of this construct is that it is minimally invasive and compression across the fracture site can be obtained^[1,36]. It also has been shown to have decreased healing time with accelerated mobilization^[19,36]. DeLee *et al*^[1] were the first to describe the use of percutaneous intramedullary screw fixation with a solid 4.5-mm malleolar screw for diaphyseal stress fractures in ten athletes. The study reported an average healing time of 7.5 wk and return to sport in an average of 8.5 wk with no postoperative complications or re-fractures^[1,2,4]. It is important to note that this study was published prior to the introduction of the Torg *et al*^[13] classification. Historically, the treatment of choice for symptomatic Torg type II and type III fractures as first described by Torg *et al*^[13], in their study that introduced the Torg classification was cortico-cancellous bone graft. In this series 95% of patients treated with cortico-cancellous bone graft had healed radiographically and clinically at a mean of 12.3 wk^[13]. Currently, the most accepted technique for nonunions is open curettage of the nonunion site followed by intramedullary screw placement^[8].

Currently, there exists a variety of intramedullary

screws a surgeon can select from for fixation of a proximal fifth metatarsal fracture. Solid and cannulated screws exist. The theoretical advantage of a cannulated screw is the precision and ease of screw placement over a guidewire^[25,37]. However, a study done by Glasgow *et al*^[38] reported the risk of re-fracture with cannulated screws. The study examined operative failure of three delayed unions, three nonunions, and five acute Jones fractures. A variety of intramedullary screws were used including: 4.0-mm cancellous, 4.5-mm malleolar, 4.5-mm cannulated screw, and a 6.5-mm cancellous screw. They concluded that intramedullary fixation with other than a 4.5-mm malleolar screw resulted in re-fracture and failure. In this same study two of the nonunions and all of the delayed unions treated with cortico-cancellous bone graft failed. They concluded failure was due to undersized cortico-cancellous grafts and incomplete reaming of the medullary canal. Additionally, early return to vigorous physical activity with the bone graft procedure and screw fixation was associated with re-fractures and delayed union^[38]. It should be noted that that in this study the definition of Jones fracture included zone two and zone three fractures. On the contrary, a more recent study by Porter *et al*^[21] described 100% union using a partially threaded cancellous 4.5 mm cannulated screw for fixation of acute zone two fractures in self-reported athletes with high satisfaction rates and no re-fractures^[21].

Pietropaoli *et al*^[37] compared the strength of 4.5-mm malleolar screws and 4.5-mm partially threaded cancellous cannulated screws in a simulated Jones fracture (zone two) cadaver model. The study reported no difference in the two screws from a biomechanical standpoint. They also found that the forces to cause displacement in both screws were much higher than the peak force experienced by the lateral aspect of the foot. Therefore, they concluded that early return to function after intramedullary screw fixation of these fractures should be considered^[37].

Portland *et al*^[25] demonstrated 100% union rate after immediate intramedullary fixation with 4.5-mm or 5.0-mm cannulated screws in acute Jones fractures (zone two) and Torg type I diaphyseal stress fractures, with an average time to union of 6.2 wk. Immediate intramedullary fixation of type II diaphyseal stress fractures resulted in 100% union and average time to union of 8.3 wk. They advocate for immediate intramedullary fixation of Jones fractures and acutely presenting Torg type I and II diaphyseal stress fractures^[25].

A more recent study done by DeSandis *et al*^[36] investigated screw sizing of zone two fractures using CT and radiographic analysis of fifth metatarsal morphology in 241 patients. The fifth metatarsal has a lateral curvature and a plantar bow and its shaft morphology is variable which makes choosing the correct screw challenging. They recommended using the largest diameter screw possible keeping in mind using a large diameter medullary screw in a narrow canal can result in diaphyseal fracture. The analysis found a range of canal widths between 2.2- and 5.9-mm and they concluded

most canals can accommodate a 4.0- or 4.5-mm diameter screw. They recommend using AP radiographs for preoperative templating of screw diameter to ensure the screw is an adequate size for the patient. Screw length they concluded should be as short as possible with 16 mm of distal threads. Based on their imaging analysis screw length should rarely be larger than 50-mm and typically should be 40-mm or less to prevent fracture distraction that can result due to the natural plantar bow of the fifth metatarsal. Additionally, special attention should be paid to larger individuals which based on their analysis were found to have more bowing. In this population excessively long screws should be avoided to reduce the risk of medial cortex perforation which may lead to fracture distraction^[36].

In some cases, tension band wiring may be favoured if there are small fragments that are not amenable to screw fixation^[32]. Sarimo *et al*^[39] treated 27 zone two fractures with tension band wiring with good results. Patients started weightbearing at three weeks and the mean time to union was 12.8 wk^[36].

Postoperatively after fixation of proximal fifth metatarsal fractures the foot should be immobilized and kept nonweightbearing. The period of nonweightbearing is 1 to 2 wk with progressive weightbearing in a short-leg walking cast or aircast for four to six weeks^[3,4,10,13,19,25]. A functional brace or foot orthoses may be worn if the patient is returning to strenuous competitive activity^[19,26]. Following inlay cortico-cancellous bone grafting the patient should be immobilized and nonweightbearing for six weeks as specified by Torg *et al*^[13].

CONCLUSION

The treatment of fifth metatarsal fractures is evolving and evidence-based medicine is directing care which can be nonoperative or operative. The choice of treatment varies by anatomical region, patient history and radiological findings. All nondisplaced fractures including stress fractures can be treated nonoperatively^[3,9,10,19]. Fifth metatarsal neck and shaft fractures may be treated with a variety of nonoperative modalities and weightbearing as tolerated^[19]. There is no definitive literature that describes the exact amount of translation and angulation that is acceptable for metatarsal neck and shaft fractures. The criteria cited is more than 10 degrees of plantar angulation or three to four millimeters of translation in any plane^[19]. Displacement greater than this, should be corrected by open reduction if closed reduction fails^[19]. The recommended treatment for nondisplaced zone one fractures is symptomatic care in a walking cast, air-boot, or compression wrap with protected weightbearing until discomfort subsides^[3,19]. Based on the current literature, less rigid immobilization and shorter period of nonweightbearing can be associated with better early functional outcomes (Table 1). These fractures should be treated operatively if displaced more than three millimeters or if more than 30% of the cubometatarsal joint is involved. The treatment of zone two and zone three

fractures is more complex because they are recognized for prolonged healing time and nonunion. Nonoperative treatment of zone two and zone three fractures includes immobilization and nonweightbearing for 6 to 8 wk or longer in the case of zone three stress fractures^[3,9]. Torg type I diaphyseal stress fractures and acute zone two fractures are managed nonoperatively, however in the highly active population operative management should be considered due faster clinical healing and return to sport^[3,4,21-24]. Zone two and zone three delayed unions may be managed operatively or nonoperatively^[3,4]. Operative intervention is recommended in the active population^[3]. Symptomatic zone two and zone three nonunions should be managed operatively^[3,4].

Evidence based decisions are difficult in this anatomic area as there is a paucity of good randomized control trials comparing treatment options. In the studies that do exist zone two and zone three fractures are often confused. In addition to fracture classification inconsistencies there are also inconsistencies with respect to chronicity of fractures and differentiating between stress fractures and an acute traumatic mechanism^[39]. Regardless, when making decisions on treatment, special attention should be paid to the athlete with operative and nonoperative approaches to treatment being outlined and the treatment modality should be based on the patient's preference.

REFERENCES

- 1 **DeLee JC**, Evans JP, Julian J. Stress fracture of the fifth metatarsal. *Am J Sports Med* 1983; **11**: 349-353 [PMID: 6638251 DOI: 10.1177/036354658301100513]
- 2 **Petrisor BA**, Ekrol I, Court-Brown C. The epidemiology of metatarsal fractures. *Foot Ankle Int* 2006; **27**: 172-174 [PMID: 16539897 DOI: 10.1177/107110070602700303]
- 3 **Lawrence SJ**, Botte MJ. Jones' fractures and related fractures of the proximal fifth metatarsal. *Foot Ankle* 1993; **14**: 358-365 [PMID: 8406253 DOI: 10.1177/107110079301400610]
- 4 **Dameron TB**. Fractures of the Proximal Fifth Metatarsal: Selecting the Best Treatment Option. *J Am Acad Orthop Surg* 1995; **3**: 110-114 [PMID: 10790659 DOI: 10.5435/00124635-199503000-00006]
- 5 **Dameron TB**. Fractures and anatomical variations of the proximal portion of the fifth metatarsal. *J Bone Joint Surg Am* 1975; **57**: 788-792 [PMID: 1099103]
- 6 **Thomas JL**, Davis BC. Three-wire fixation technique for displaced fifth metatarsal base fractures. *J Foot Ankle Surg* 2011; **50**: 776-779 [PMID: 21908207 DOI: 10.1053/j.jfas.2011.07.009]
- 7 **Jones R. I.** Fracture of the Base of the Fifth Metatarsal Bone by Indirect Violence. *Ann Surg* 1902; **35**: 697-700.2 [PMID: 17861128]
- 8 **Armagan OE**, Shereff MJ. Injuries to the toes and metatarsals. *Orthop Clin North Am* 2001; **32**: 1-10 [PMID: 11465121 DOI: 10.1016/S0030-5898(05)70189-9]
- 9 **Rammelt S**, Heineck J, Zwipp H. Metatarsal fractures. *Injury* 2004; **35** Suppl 2: SB77-SB86 [PMID: 15315882 DOI: 10.1016/j.injury.2004.07.016]
- 10 **Zwitser EW**, Breederveld RS. Fractures of the fifth metatarsal: diagnosis and treatment. *Injury* 2010; **41**: 555-562 [PMID: 19570536 DOI: 10.1016/j.injury.2009.05.035]
- 11 **Stewart IM**. Jones's fracture: fracture of base of fifth metatarsal. *Clin Orthop* 1960; **16**: 190-198 [PMID: 13834594]
- 12 **Smith JW**, Arnoczky SP, Hersh A. The intraosseous blood supply of the fifth metatarsal: implications for proximal fracture healing. *Foot Ankle* 1992; **13**: 143-152 [PMID: 1601342 DOI: 10.1177/107110079201300306]
- 13 **Torg JS**, Balduini FC, Zelko RR, Pavlov H, Peff TC, Das M. Fractures of the base of the fifth metatarsal distal to the tuberosity. Classification and guidelines for non-surgical and surgical management. *J Bone Joint Surg Am* 1984; **66**: 209-214 [PMID: 6693447]
- 14 **Dean BJ**, Kothari A, Uppal H, Kankate R. The Jones fracture classification, management, outcome, and complications: a systematic review. *Foot Ankle Spec* 2012; **5**: 256-259 [PMID: 22547534 DOI: 10.1177/1938640012444730]
- 15 **Roche AJ**, Calder JD. Treatment and return to sport following a Jones fracture of the fifth metatarsal: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1307-1315 [PMID: 22956165 DOI: 10.1007/s00167-012-2138-8]
- 16 **Lehman RC**, Torg JS, Pavlov H, DeLee JC. Fractures of the base of the fifth metatarsal distal to the tuberosity: a review. *Foot Ankle* 1987; **7**: 245-252 [PMID: 3817669 DOI: 10.1177/107110078700700406]
- 17 **Zwipp H**, Ranft T. [Malunited juvenile fractures in the foot region]. *Orthopade* 1991; **20**: 374-380 [PMID: 1684652]
- 18 **Mehlhorn AT**, Zwingmann J, Hirschmüller A, Südkamp NP, Schmal H. Radiographic classification for fractures of the fifth metatarsal base. *Skeletal Radiol* 2014; **43**: 467-474 [PMID: 24442562 DOI: 10.1007/s00256-013-1810-5]
- 19 **Fetzer GB**, Wright RW. Metatarsal shaft fractures and fractures of the proximal fifth metatarsal. *Clin Sports Med* 2006; **25**: 139-150, x [PMID: 16324980 DOI: 10.1016/j.csm.2005.08.014]
- 20 **Chuckpaiwong B**, Queen RM, Easley ME, Nunley JA. Distinguishing Jones and proximal diaphyseal fractures of the fifth metatarsal. *Clin Orthop Relat Res* 2008; **466**: 1966-1970 [PMID: 18363075 DOI: 10.1007/s11999-008-0222-7]
- 21 **Porter DA**, Duncan M, Meyer SJ. Fifth metatarsal Jones fracture fixation with a 4.5-mm cannulated stainless steel screw in the competitive and recreational athlete: a clinical and radiographic evaluation. *Am J Sports Med* 2005; **33**: 726-733 [PMID: 15722272 DOI: 10.1177/0363546504271000]
- 22 **Mindrebo N**, Shelbourne KD, Van Meter CD, Rettig AC. Outpatient percutaneous screw fixation of the acute Jones fracture. *Am J Sports Med* 1993; **21**: 720-723 [PMID: 8238714 DOI: 10.1177/036354659302100514]
- 23 **Quill GE**. Fractures of the proximal fifth metatarsal. *Orthop Clin North Am* 1995; **26**: 353-361 [PMID: 7724197]
- 24 **Mologne TS**, Lundeen JM, Clapper MF, O'Brien TJ. Early screw fixation versus casting in the treatment of acute Jones fractures. *Am J Sports Med* 2005; **33**: 970-975 [PMID: 15888715 DOI: 10.1177/0363546504272262]
- 25 **Portland G**, Kelikian A, Kodros S. Acute surgical management of Jones' fractures. *Foot Ankle Int* 2003; **24**: 829-833 [PMID: 14655886]
- 26 **Raikin SM**, Slenker N, Ratigan B. The association of a varus hindfoot and fracture of the fifth metatarsal metaphyseal-diaphyseal junction: the Jones fracture. *Am J Sports Med* 2008; **36**: 1367-1372 [PMID: 18443278 DOI: 10.1177/0363546508314401]
- 27 **Aynardi M**, Pedowitz DI, Saffel H, Piper C, Raikin SM. Outcome of nonoperative management of displaced oblique spiral fractures of the fifth metatarsal shaft. *Foot Ankle Int* 2013; **34**: 1619-1623 [PMID: 23908388 DOI: 10.1177/1071100713500656]
- 28 **O'Malley MJ**, Hamilton WG, Munyak J. Fractures of the distal shaft of the fifth metatarsal. "Dancer's fracture". *Am J Sports Med* 1996; **24**: 240-243 [PMID: 8775129 DOI: 10.1177/036354659602400223]
- 29 **Shahid MK**, Punwar S, Boulind C, Bannister G. Aircast walking boot and below-knee walking cast for avulsion fractures of the base of the fifth metatarsal: a comparative cohort study. *Foot Ankle Int* 2013; **34**: 75-79 [PMID: 23386764 DOI: 10.1177/1071100712460197]
- 30 **Clapper MF**, O'Brien TJ, Lyons PM. Fractures of the fifth metatarsal. Analysis of a fracture registry. *Clin Orthop Relat Res* 1995; **318**: 238-241 [PMID: 7634674]
- 31 **Gray AC**, Rooney BP, Ingram R. A prospective comparison of two treatment options for tuberosity fractures of the proximal fifth metatarsal. *Foot (Edinb)* 2008; **18**: 156-158 [PMID: 20307430 DOI: 10.1016/j.foot.2008.02.002]
- 32 **Wiener BD**, Linder JF, Giattini JF. Treatment of fractures of the fifth metatarsal: a prospective study. *Foot Ankle Int* 1997; **18**: 267-269

Bowes J *et al.* Review of fifth metatarsal fractures

- [PMID: 9167925 DOI: 10.1177/107110079701800504]
- 33 **Konkel KF**, Menger AG, Retzlaff SA. Nonoperative treatment of fifth metatarsal fractures in an orthopaedic suburban private multispecialty practice. *Foot Ankle Int* 2005; **26**: 704-707 [PMID: 16174500 DOI: 10.1177/107110070502600907]
- 34 **Cakir H**, Van Vliet-Koppert ST, Van Lieshout EM, De Vries MR, Van Der Elst M, Schepers T. Demographics and outcome of metatarsal fractures. *Arch Orthop Trauma Surg* 2011; **131**: 241-245 [PMID: 20714904 DOI: 10.1007/s00402-010-1164-6]
- 35 **Tahririan MA**, Momeni A, Moayednia A, Yousefi E. Designing a prognostic scoring system for predicting the outcomes of proximal fifth metatarsal fractures at 20 weeks. *Iran J Med Sci* 2015; **40**: 104-109 [PMID: 25821289]
- 36 **DeSandis B**, Murphy C, Rosenbaum A, Levitsky M, O'Malley Q, Konin G, Drakos M. Multiplanar CT Analysis of Fifth Metatarsal Morphology: Implications for Operative Management of Zone II Fractures. *Foot Ankle Int* 2016; **37**: 528-536 [PMID: 26678426 DOI: 10.1177/1071100715623041]
- 37 **Pietropaoli MP**, Wnorowski DC, Werner FW, Fortino MD. Intramedullary screw fixation of Jones fractures: a biomechanical study. *Foot Ankle Int* 1999; **20**: 560-563 [PMID: 10509682 DOI: 10.1177/107110079902000904]
- 38 **Glasgow MT**, Naranja RJ, Glasgow SG, Torg JS. Analysis of failed surgical management of fractures of the base of the fifth metatarsal distal to the tuberosity: the Jones fracture. *Foot Ankle Int* 1996; **17**: 449-457 [PMID: 8863022 DOI: 10.1177/107110079601700803]
- 39 **Sarimo J**, Rantanen J, Orava S, Alanen J. Tension-band wiring for fractures of the fifth metatarsal located in the junction of the proximal metaphysis and diaphysis. *Am J Sports Med* 2006; **34**: 476-480 [PMID: 16303878 DOI: 10.1177/0363546505281803]

P- Reviewer: Erdil M, Vulcano E, Zheng N **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Lu YJ



Basic Study

Extrinsic visual feedback and additional cognitive/physical demands affect single-limb balance control in individuals with ankle instability

You-jou Hung, Jacob Miller

You-jou Hung, Jacob Miller, Department of Physical Therapy, Angelo State University, San Angelo, TX 76909, United States

Author contributions: Hung Y analyzed the data; Hung Y wrote the paper; Hung Y and Miller J designed the research; Miller J performed the research.

Institutional review board statement: The study was reviewed and approved by the Angelo State University Institutional Review Board.

Institutional animal care and use committee statement: NA.

Conflict-of-interest statement: No potential conflict-of-interest relevant to the manuscript.

Data sharing statement: Consent for data sharing was not obtained but the presented data are anonymized and risk of identification is low.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: You-jou Hung, PT, MS, PhD, CSCS, Department of Physical Therapy, Angelo State University, ASU Station #10923, San Angelo, TX 76909, United States. you-jou.hung@angelo.edu
Telephone: +1-325-9422742
Fax: +1-325-9422548

Received: July 18, 2016

Peer-review started: July 21, 2016

First decision: September 5, 2016

Revised: September 6, 2016

Accepted: October 5, 2016

Article in press: October 7, 2016

Published online: December 18, 2016

Abstract

AIM

To investigate the impact of extrinsic visual feedback and additional cognitive/physical demands on single-limb balance in individuals with ankle instability.

METHODS

Sixteen subjects with ankle instability participated in the study. Ankle instability was identified using the Cumberland Ankle Instability Tool (CAIT). The subject's unstable ankle was examined using the Athletic Single Leg Stability Test of the Biodex Balance System with 4 different protocols: (1) default setting with extrinsic visual feedback from the monitor; (2) no extrinsic visual feedback; (3) no extrinsic visual feedback with cognitive demands; and (4) no extrinsic visual feedback with physical demands. For the protocol with added cognitive demands, subjects were asked to continue subtracting 7 from a given number while performing the same test without extrinsic visual feedback. For the protocol with added physical demands, subjects were asked to pass and catch a basketball to and from the examiner while performing the same modified test.

RESULTS

The subject's single-limb postural control varied significantly among different testing protocols ($F = 103$; $P = 0.000$). Subjects' postural control was the worst with added physical demands and the best with the default condition with extrinsic visual feedback. Pairwise

comparison shows subjects performed significantly worse in all modified protocols ($P < 0.01$ in all comparisons) compared to the default protocol. Results from all 4 protocols are significantly different from each other ($P < 0.01$) except for the comparison between the “no extrinsic visual feedback” and “no extrinsic visual feedback with cognitive demands” protocols. Comparing conditions without extrinsic visual feedback, adding a cognitive demand did not significantly compromise single-limb balance control but adding a physical demand did. Scores from the default protocol are significantly correlated with the results from all 3 modified protocols: No extrinsic visual feedback ($r = 0.782$; $P = 0.000$); no extrinsic visual feedback with cognitive demands ($r = 0.569$; $P = 0.022$); no extrinsic visual feedback with physical demands ($r = 0.683$; $P = 0.004$). However, the CAIT score is not significantly correlated with the single-limb balance control from any of the 4 protocols: Default with extrinsic visual feedback ($r = -0.210$; $P = 0.434$); no extrinsic visual feedback ($r = -0.450$; $P = 0.081$); no extrinsic visual feedback with cognitive demands ($r = -0.406$; $P = 0.118$); no extrinsic visual feedback with physical demands ($r = -0.351$; $P = 0.182$).

CONCLUSION

Single-limb balance control is worse without extrinsic visual feedback and/or with cognitive/physical demands. The balance test may not be a valid tool to examine ankle instability.

Key words: Ankle; Balance; Instability; Motor control; Rehabilitation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Single-limb balance control with the Biodex Balance System (BBS) was significantly worse without extrinsic visual feedback and with cognitive or physical demands in those with ankle instability. Clinicians should consider a patient’s activity and incorporate proper additional demands in ankle stability testing. In addition, the Athletic Single Leg Stability Test of the BBS may not be a valid tool to examine ankle instability. Further research is needed to examine the validity and reliability of the Athletic Single Leg Stability Test in testing ankle instability.

Hung Y, Miller J. Extrinsic visual feedback and additional cognitive/physical demands affect single-limb balance control in individuals with ankle instability. *World J Orthop* 2016; 7(12): 801-807 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/801.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.801>

INTRODUCTION

Ankle sprain is one of the most common musculoskeletal injuries, especially for active individuals and athletes^[1-3]. An estimated 23000 ankle sprains occur daily in the

United States alone^[1]. Ankle sprains often occur as the result of trauma (e.g., landing on an uneven surface from a jump), compromising the physical structural and functional integrity of the tissues surrounding the joint^[4]. It was reported that lateral ankle sprains comprise up to 83% of all ankle injuries^[5]. They are likely the result of a fast perturbation of ankle plantar flexion and inversion, contributing to complete or partial tears of the 3 lateral ankle ligaments (anterior talo-fibular ligament, calcaneo-fibular ligament, and posterior talo-fibular ligament). Moreover, compromised mechanical restraints (e.g., injured ligaments, joint capsule), muscle strength, and/or neuromuscular control (e.g., proprioception deficits) after the initial injury may further compromise ankle stability^[6-18]. As the result, 73% of the individuals who had sprained their ankles before are likely to experience recurrent injuries and ankle instability^[19].

Several screening tools [e.g., The Cumberland Ankle Instability Tool (CAIT), The Ankle Instability Instrument, The Functional Ankle Instability Questionnaire] have been developed to identify individuals with ankle instability^[18]. A panel of experts concluded that CAIT is based on the highest level (level I) of evidence according to guidelines described by the Centre of Evidence-Based Medicine, Oxford, United Kingdom^[18]. The CAIT is a 9-item questionnaire with the score ranges from 30 (best) to 0 (worst)^[19]. A subject scores lower than 28 would be considered having ankle instability. It has a test-retest intraclass correlation coefficient (ICC) of 0.96, and it also has a good sensitivity (82.9) and specificity (74.7) in differentiating participants with or without ankle instability^[19].

Proper balance control is crucial to ensure safe functional activities. It is achieved with the integration of sensory inputs (e.g., visual, vestibular, and somatosensory information), muscle activations, and cognitive function in human bodies^[20]. For individuals with ankle instability, compromised muscle strength and proprioception around the ankle joint may hamper balance control^[21,22]. A variety of laboratory equipment (e.g., force plates) and clinical tests (e.g., Y Balance Test, Star Excursion Balance Test, Foot Lift Test) have been developed to examine balance control. One of the commonly used devices to examine both static and dynamic balance control is the Biodex Balance System (BBS; Biodex, Inc, Shirley, NY)^[23]. This apparatus has a good test-retest reliability and provides quantitative measures of balance control^[24,25]. In addition, the BBS uses a multi-axial testing platform which can be set at various degrees of instability/difficulty (from the static protocol of 0° surface tilt to a dynamic protocol of 20° surface tilt) to challenge the subjects with various fitness levels and injury severities^[25]. Compared to other balance testing equipment, the unstable platform of the BBS can simulate unexpected external perturbations (such as landing on an uneven surface) in various activities. However, the monitor of the BBS also provides extrinsic visual feedback (information about the center of gravity location in relation to the base of support) to the subject and compromises the test’s functional significance. In real life scenarios, individuals don’t receive concurrent visual

information about their performance. Therefore, balance control measured with the BBS may not truly reflect balance control in daily activities.

Individuals often sprain their ankles while engaging a sport activity (*e.g.*, basketball), in which additional cognitive demands (*e.g.*, whom to pass the ball to) and/or physical demands (*e.g.*, catching or passing the ball) are often present. It was suggested that balance activities take place in association with at least one concurrent task in daily activities, and cognitive function can have an impact on balance control^[26]. The impact of adding a cognitive loading on functional activities such as gait and balance control is inconclusive, depending on many factors such as the difficulty of the primary/secondary tasks and subject conditions^[26-34]. Examining single-leg balance control with the BBS, Rahnama *et al.*^[30] (2010) reported adding a cognitive task decreased postural stability in subjects with ankle instability. However, they used a modified protocol with their subjects' eyes closed during the testing. Eliminating all visual inputs does not resemble functional activities and common ankle injury mechanisms. Moreover, their protocol can further increase anxiety and unnecessary muscle activation, therefore compromising balance control. In addition, no study had examined the impact of adding a physical demand with a functional significance to individuals performing the single-leg balance test with the BBS.

The first aim of this study was to investigate the impact of extrinsic visual feedback and additional cognitive/physical demands on single-limb balance in individuals with ankle instability. The second aim of the study was to investigate if any of the 4 single-limb balance testing protocols correlates to ankle stability measured by the CAIT. It was hypothesized that taking away the extrinsic feedback and additional cognitive/physical demands could compromise single-limb balance control. Results of the study can provide clinicians useful information regarding testing and rehabilitation regimens for individuals with ankle instability.

MATERIALS AND METHODS

Participants

Sixteen subjects (12 females and 4 males, ranged from 19-30 years old) with ankle instability participated in the study. Subjects were recruited from the campus of a local university. The inclusion criteria for the subjects includes: (1) have one or more ankle sprains over the same ankle resulted in pain, swelling, and/or loss of function when it occurred; (2) have the latest ankle sprain occurred within the past year; (3) have no other prior injury that received medical attention for the injured ankle; (4) have no pain or discomfort during single leg standing over the injured ankle at participation; and (5) answer "no" to all questions on the Physical Activity Readiness Questionnaire (PAR-Q and YOU)^[35]. All participants signed a consent form approved by the Institutional Review Board of the local university at the beginning of the study.

Procedures

At the beginning of the testing session, subjects were asked to fill out the CAIT questionnaire (Table 1). Only subjects who scored 27 or less (an indication of ankle instability) were asked to participate in the study. The subject's unstable ankle was examined using the Athletic Single Leg Stability Test of the BBS. The single-leg test was chosen because all subjects were recreational athletes and other double foot support and/or static protocols of the BBS lack functional significance. Subjects were examined with 4 different protocols: (1) default setting with extrinsic visual feedback; (2) no extrinsic visual feedback; (3) no extrinsic visual feedback with cognitive demands; and (4) no extrinsic visual feedback with physical demands (Figure 1). Subjects were tested at dynamic level 4, which provided moderate balance control difficulty.

After adopting a single-limb stance on the BSS platform without shoes, subjects performed a total of 3 trials with 20 s/trial while receiving extrinsic visual feedback (their center of gravity location in relation to the base of support) concurrently from the monitor. For the remaining 3 modified protocols, subjects were positioned on the platform facing the opposite direction while keeping the same relative foot position/alignment in relation to the platform as in the default protocol. In the modified protocols, subjects were able to use vision to assist maintaining the balance but without the direct extrinsic visual feedback from the monitor. For the protocol with cognitive demands, subjects were asked to continue subtracting 7 from 121 (trial 1), 119 (trial 2), and 116 (trial 3) to 0 without feedback from the monitor. For the protocol with physical demands, subjects were asked to pass and catch a basketball to and from an examiner standing 6 feet away. The pace was standardized at once every second (guided by a metronome). All 3 modified protocols consisted of 3 trials with 20 s/trial. Subjects were asked to sit and relax for 2 min between protocols to avoid fatigue.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics (Armonk, NY) Version 21.0. The overall stability index (OSI) produced by the BBS was used for analyses. One-way Analysis of Variance (ANOVA) with repeated measures was used to compare the 4 different testing protocols. Post hoc comparisons were performed with the Paired-Samples *T* test. Pearson Correlation was used to examine the correlations between the OSI and the CAIT scores. Significance level (*P*-values) was set at 0.05 for all comparisons.

RESULTS

The subject's single-limb balance control varied significantly among different protocols ($F = 103$; $P = 0.000$). Subjects' postural control was the worst with added physical demand (passing and catching a basketball) and the best

Table 1 The Cumberland Ankle Instability Tool

Please check the one statement in each question that best describes your ankles			
	Left	Right	Score
1 I have pain in my ankle			
Never	<input type="checkbox"/>	<input type="checkbox"/>	5
During sport	<input type="checkbox"/>	<input type="checkbox"/>	4
Running on uneven surfaces	<input type="checkbox"/>	<input type="checkbox"/>	3
Running on level surfaces	<input type="checkbox"/>	<input type="checkbox"/>	2
Walking on uneven surfaces	<input type="checkbox"/>	<input type="checkbox"/>	1
Walking on level surfaces	<input type="checkbox"/>	<input type="checkbox"/>	0
2 My ankle feels unstable			
Never	<input type="checkbox"/>	<input type="checkbox"/>	4
Sometimes during sport (not every time)	<input type="checkbox"/>	<input type="checkbox"/>	3
Frequently during sport (every time)	<input type="checkbox"/>	<input type="checkbox"/>	2
Sometimes during daily activity	<input type="checkbox"/>	<input type="checkbox"/>	1
Frequently during daily activity	<input type="checkbox"/>	<input type="checkbox"/>	0
3 When I make SHARP turns, my ankle feels unstable			
Never	<input type="checkbox"/>	<input type="checkbox"/>	3
Sometimes when running	<input type="checkbox"/>	<input type="checkbox"/>	2
Often when running	<input type="checkbox"/>	<input type="checkbox"/>	1
When walking	<input type="checkbox"/>	<input type="checkbox"/>	0
4 When going down the stairs, my ankle feels unstable			
Never	<input type="checkbox"/>	<input type="checkbox"/>	3
If I go fast	<input type="checkbox"/>	<input type="checkbox"/>	2
Occasionally	<input type="checkbox"/>	<input type="checkbox"/>	1
Always	<input type="checkbox"/>	<input type="checkbox"/>	0
5 My ankle feels unstable when standing on one leg			
Never	<input type="checkbox"/>	<input type="checkbox"/>	2
On the ball of my foot	<input type="checkbox"/>	<input type="checkbox"/>	1
With my foot flat	<input type="checkbox"/>	<input type="checkbox"/>	0
6 My ankle feels unstable when			
Never	<input type="checkbox"/>	<input type="checkbox"/>	3
I hop from side to side	<input type="checkbox"/>	<input type="checkbox"/>	2
I hop on the spot	<input type="checkbox"/>	<input type="checkbox"/>	1
When I jump	<input type="checkbox"/>	<input type="checkbox"/>	0
7 My ankle feels unstable when			
Never	<input type="checkbox"/>	<input type="checkbox"/>	4
I run on uneven surfaces	<input type="checkbox"/>	<input type="checkbox"/>	3
I jog on uneven surfaces	<input type="checkbox"/>	<input type="checkbox"/>	2
I walk on uneven surfaces	<input type="checkbox"/>	<input type="checkbox"/>	1
I walk on a flat surface	<input type="checkbox"/>	<input type="checkbox"/>	0
8 Typically, when I start to roll over (or "twist") on my ankle, I can stop it			
Immediately	<input type="checkbox"/>	<input type="checkbox"/>	3
Often	<input type="checkbox"/>	<input type="checkbox"/>	2
Sometimes	<input type="checkbox"/>	<input type="checkbox"/>	1
Never	<input type="checkbox"/>	<input type="checkbox"/>	0
I have never rolled over on my ankle	<input type="checkbox"/>	<input type="checkbox"/>	3
9 After a typical incident of my ankle rolling over, my ankle returns to "normal"			
Almost immediately	<input type="checkbox"/>	<input type="checkbox"/>	3
Less than one day	<input type="checkbox"/>	<input type="checkbox"/>	2
1-2 d	<input type="checkbox"/>	<input type="checkbox"/>	1
More than 2 d	<input type="checkbox"/>	<input type="checkbox"/>	0
I have never rolled over on my ankle	<input type="checkbox"/>	<input type="checkbox"/>	3

with the default condition with extrinsic visual feedback (Figure 2). Pairwise comparison shows subjects performed significantly worse in all modified protocols ($P < 0.01$ in all comparisons) compared to the default protocol. Results from all 4 protocols are significantly different from each other ($P < 0.01$), except for the comparison between the "no extrinsic visual feedback" and "no extrinsic visual feedback with cognitive demands" protocols. Comparing conditions without extrinsic visual feedback, adding a cognitive demand did not significantly compromise single-limb balance control but adding a physical demand did.

Scores from the default protocol are significantly correlated with the results from all 3 modified protocols: no extrinsic visual feedback ($r = 0.782$; $P = 0.000$); no extrinsic visual feedback with cognitive demands ($r = 0.569$; $P = 0.022$); no extrinsic visual feedback with physical demands ($r = 0.683$; $P = 0.004$). However, the CAIT score is not significantly correlated with the OSI from any of the 4 protocols: default with extrinsic visual feedback ($r = -0.210$; $P = 0.434$); no extrinsic visual feedback ($r = -0.450$; $P = 0.081$); no extrinsic visual feedback with cognitive demands ($r = -0.406$; $P = 0.118$); no extrinsic

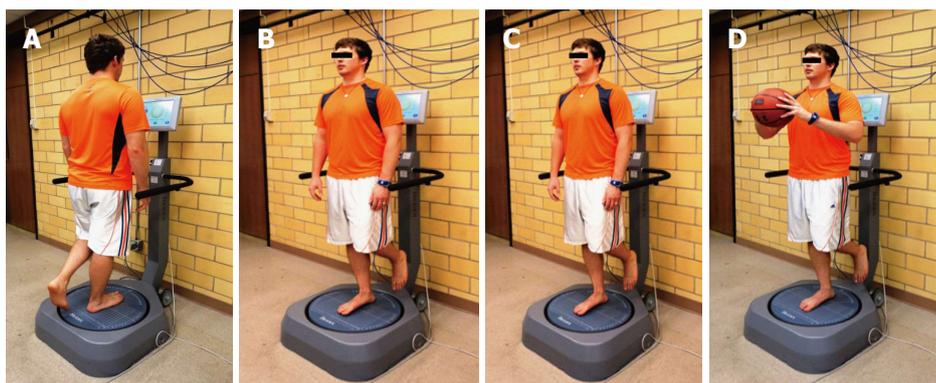


Figure 1 Single-limb balance testing protocols with the Biodex Balance System. A: The Athletic Single Leg Stability Test (default) with extrinsic visual feedback from the monitor; B: Modified test without extrinsic visual feedback; C: Modified test without extrinsic visual feedback and with cognitive demands; D: Modified test without extrinsic visual feedback and with physical demands.

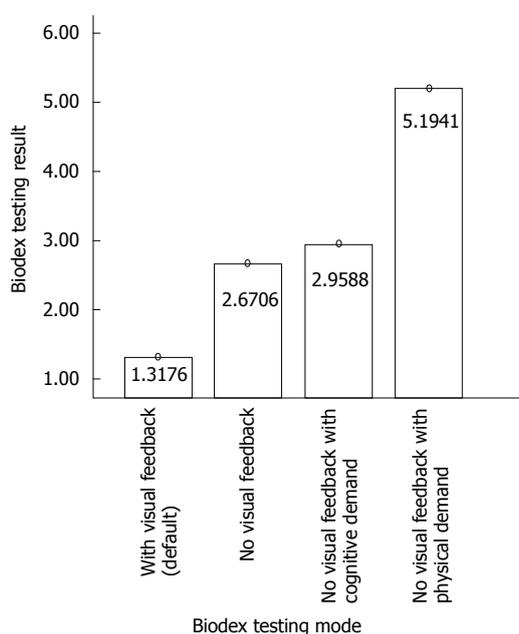


Figure 2 Overall stability Index of the Biodex Balance System from the 4 testing protocols.

visual feedback with physical demands ($r = -0.351$; $P = 0.182$).

DISCUSSION

Compared to the default setting, results of the present study show single-limb balance control was significantly worse without extrinsic visual feedback with the BBS. The BBS is a common testing and training apparatus for balance control. However, the monitor of the BBS provides concurrent extrinsic visual feedback about the performance, which is not available in most activities. In other words, performance with the BBS may overestimate the true capability of balance control in a functional setting. Although providing additional extrinsic visual feedback could be beneficial during training sessions for those with balance control deficits (e.g., patients with severe Parkinson disease), its result may not accurately

reflect the performance in other conditions without additional visual feedback. Moreover, individuals who train exclusively with the BBS may grow accustomed to rely too much on extrinsic visual cues for balance control.

The results show that adding a cognitive demand did not significantly compromise single-limb balance control with the BBS. Literature is very limited about the role of cognitive function on balance control for individuals with ankle instability^[30]. The impact of adding a cognitive loading on functional activities depends on many factors such as the difficulty of the primary/secondary tasks and subject conditions^[26-34]. Rahnama *et al.*^[30] (2010) reported that adding a cognitive task decreased single-limb postural stability in subjects with ankle instability. However, their subjects were asked to close their eyes during the testing. Despite not having extrinsic visual feedbacks, subjects in the current study could still use their vision in a subconscious matter to adjust their body alignment in relation to surrounding objects. Therefore, an easier primary task (maintaining the balance) may explain the lack of cognitive effect in the current study. Another explanation for the difference between the two projects is the difficulty of the secondary task. Instead of performing a simple mathematic calculation task, their subjects were asked to remember the sequence of 7 digits and then repeat the digits in the exact reverse order. The more difficult secondary task could also have a greater impact on single-limb balance control in their study.

No study had examined the impact of adding physical demands on single-limb balance control in individuals with ankle instability. Considering basketball players are more vulnerable to ankle sprains (41.1% prevalence) than other athletes^[3], the present study adopted a physical demand (catching and passing) that is similar to playing basketball. The results show that adding a physical demand significantly compromised single-limb balance control with the BBS. In order to catch and pass the basketball properly in a timely fashion, subjects could not solely focus on balance control. Engaging an upper extremity movement/perturbation also moved their center of gravity away from the base of support more

often, therefore making it more challenging to maintain single-limb balance. Based on the results, clinicians should incorporate physical demands in ankle stability testing and rehabilitation protocols to better simulate functional activities and sports.

Results of the present study indicate a poor correlation between single-limb balance control and ankle instability severity. It was suggested that ankle instability can have a negative impact on balance control^[21,22]. Because after the initial ankle sprain, overstretched ligaments and joint capsule may hamper the function of mechanoreceptors (*e.g.*, muscles spindles and Golgi Tendon Organs) and compromise the proprioception of the ankle joint^[6-18]. However, other studies found no proprioception difference between unstable and healthy ankles^[10,36-38]. Moreover, balance control can also rely on other motor control strategies (*e.g.*, hip strategy), and the coordination of other joints (*e.g.*, hip and knee) and muscles (*e.g.*, trunk muscles). In conclusion, many factors other than ankle stability can contribute to single-limb balance control. The results of the current study suggest that OSI measured with the BBS may not be a good indicator of the severity of ankle instability.

A limitation of the present study is the small sample size. In addition, future studies may consider adding a separate group of subjects without ankle instability to examine if subjects with ankle instability respond to added demands differently from healthy subjects. Although the BBS is a commonly used apparatus in a rehabilitation setting, further research is needed to examine the validity and reliability of the Athletic Single Leg Stability Test in testing ankle instability.

Single-limb balance control is compromised without extrinsic visual feedback and/or with added cognitive/physical demands. Clinicians should consider eliminating excessive extrinsic visual feedback and incorporating physical demands in ankle stability testing and rehabilitation protocols to better simulate functional activities and sports. In addition, many factors other than ankle stability may impact single-limb balance control. Single-limb balance tests with the BBS may not be a valid tool to categorize the severity of ankle instability.

COMMENTS

Background

Ankle sprain is one of the most common musculoskeletal injuries. Recurrent ankle sprains can cause ankle instability, and potentially contribute to poor balance control. The purpose of the research was to examine the impact of extrinsic visual feedback and additional cognitive/physical demands on single-limb balance control, and to examine if those testing results can correlate to the severity of ankle instability.

Research frontiers

Ankle instability is a well-studied pathology. However, it is still unclear if ankle instability would have a significant impact on single-limb balance control. In addition, some of the commonly used balance testing protocols provide too much visual feedback and lack functional significance.

Innovations and breakthroughs

In order to provide more functional significance of a commonly used protocol for

single-limb balance testing, the default protocol was modified to better resemble daily activities and sport movements.

Applications

Clinicians should consider eliminating excessive extrinsic visual feedback and incorporating physical demands in ankle stability testing and rehabilitation protocols to better simulate functional activities and sports.

Terminology

Extrinsic visual feedback in the current study refers to the visual information about the center of gravity location in relation to the base of support displayed by the Biodex Balance System monitor. Proprioception includes both position sense and movement sense of a joint.

Peer-review

Authors aimed to investigate the impact of extrinsic visual feedback and additional cognitive/physical demands on single-limb balance in individuals with ankle instability. Sixteen subjects with ankle instability participated in the study.

REFERENCES

- 1 **Kannus P**, Renström P. Treatment for acute tears of the lateral ligaments of the ankle. Operation, cast, or early controlled mobilization. *J Bone Joint Surg Am* 1991; **73**: 305-312 [PMID: 1993726]
- 2 **Farrer C**, Franck N, Paillard J, Jeannerod M. The role of proprioception in action recognition. *Conscious Cogn* 2003; **12**: 609-619 [PMID: 14656504 DOI: 10.1016/S1053-8100(03)00047-3]
- 3 **Waterman BR**, Owens BD, Davey S, Zacchilli MA, Belmont PJ. The epidemiology of ankle sprains in the United States. *J Bone Joint Surg Am* 2010; **92**: 2279-2284 [PMID: 20926721 DOI: 10.2106/JBJS.1.01537]
- 4 **Sueki D**, Jacklyn B. Orthopedic Rehabilitation Clinical Advisor. 1st ed. USA: Mosby Elsevier, 2010: 624-625
- 5 **Fong DT**, Hong Y, Chan LK, Yung PS, Chan KM. A systematic review on ankle injury and ankle sprain in sports. *Sports Med* 2007; **37**: 73-94 [PMID: 17190537 DOI: 10.1177/107110079001100108]
- 6 **Akbari M**, Karimi H, Farahini H, Faghihzadeh S. Balance problems after unilateral lateral ankle sprains. *J Rehabil Res Dev* 2006; **43**: 819-824 [PMID: 17436168 DOI: 10.1682/JRRD.2006.01.0001]
- 7 **Arnold BL**, De La Motte S, Linens S, Ross SE. Ankle instability is associated with balance impairments: a meta-analysis. *Med Sci Sports Exerc* 2009; **41**: 1048-1062 [PMID: 19346982 DOI: 10.1249/MSS.0b013e318192d044]
- 8 **Fu AS**, Hui-Chan CW. Ankle joint proprioception and postural control in basketball players with bilateral ankle sprains. *Am J Sports Med* 2005; **33**: 1174-1182 [PMID: 16000667 DOI: 10.1177/0363546504271976]
- 9 **Freeman MA**, Dean MR, Hanham IW. The etiology and prevention of functional instability of the foot. *J Bone Joint Surg Br* 1965; **47**: 678-685 [PMID: 5846767]
- 10 **de Noronha M**, Refshauge KM, Kilbreath SL, Crosbie J. Loss of proprioception or motor control is not related to functional ankle instability: an observational study. *Aust J Physiother* 2007; **53**: 193-198 [PMID: 17725477 DOI: 10.1016/S0004-9514(07)70027-2]
- 11 **McKeon JM**, McKeon PO. Evaluation of joint position recognition measurement variables associated with chronic ankle instability: a meta-analysis. *J Athl Train* 2012; **47**: 444-456 [PMID: 22889661 DOI: 10.4085/1062-6050-47.4.15]
- 12 **Munn J**, Sullivan SJ, Schneiders AG. Evidence of sensorimotor deficits in functional ankle instability: a systematic review with meta-analysis. *J Sci Med Sport* 2010; **13**: 2-12 [PMID: 19442581 DOI: 10.1016/j.jsams.2009.03.004]
- 13 **de Noronha M**, Refshauge KM, Herbert RD, Kilbreath SL, Hertel J. Do voluntary strength, proprioception, range of motion, or postural sway predict occurrence of lateral ankle sprain? *Br J Sports Med* 2006; **40**: 824-828; discussion 828 [PMID: 16920769 DOI: 10.1136/bjsm.2006.029645]
- 14 **Payne KA**, Berg K, Latin RW. Ankle injuries and ankle strength,

- flexibility, and proprioception in college basketball players. *J Athl Train* 1997; **32**: 221-225 [PMID: 16558453]
- 15 **Willems T**, Witvrouw E, Verstuyft J, Vaes P, De Clercq D. Proprioception and Muscle Strength in Subjects With a History of Ankle Sprains and Chronic Instability. *J Athl Train* 2002; **37**: 487-493 [PMID: 12937572]
 - 16 **Witchalls J**, Waddington G, Blanch P, Adams R. Ankle instability effects on joint position sense when stepping across the active movement extent discrimination apparatus. *J Athl Train* 2012; **47**: 627-634 [PMID: 23182010 DOI: 10.4085/1062-6050-47.6.12]
 - 17 **Refshauge KM**, Kilbreath SL, Raymond J. Deficits in detection of inversion and eversion movements among subjects with recurrent ankle sprains. *J Orthop Sports Phys Ther* 2003; **33**: 166-173; discussion 173-176 [PMID: 12723673 DOI: 10.2519/jospt.2003.33.4.166]
 - 18 **Martin RL**, Davenport TE, Paulseth S, Wukich DK, Godges JJ. Ankle stability and movement coordination impairments: ankle ligament sprains. *J Orthop Sports Phys Ther* 2013; **43**: A1-40 [PMID: 24313720 DOI: 10.2519/jospt.2013.0305]
 - 19 **Hiller CE**, Refshauge KM, Bundy AC, Herbert RD, Kilbreath SL. The Cumberland ankle instability tool: a report of validity and reliability testing. *Arch Phys Med Rehabil* 2006; **87**: 1235-1241 [PMID: 16935061 DOI: 10.1016/j.apmr.2006.05.022]
 - 20 **Emery CA**. Is there a clinical standing balance measurement appropriate for use in sports medicine? A review of the literature. *J Sci Med Sport* 2003; **6**: 492-504 [PMID: 14723398 DOI: 10.1016/S1440-2440(03)80274-8]
 - 21 **Tropp H**, Odenrick P. Postural control in single-limb stance. *J Orthop Res* 1988; **6**: 833-839 [PMID: 3171763 DOI: 10.1002/jor.1100060607]
 - 22 **Riemann BL**. Is There a Link Between Chronic Ankle Instability and Postural Instability? *J Athl Train* 2002; **37**: 386-393 [PMID: 12937560]
 - 23 **Cug M**, Wikstrom EA. Learning effects associated with the least stable level of the biodex® stability system during dual and single limb stance. *J Sports Sci Med* 2014; **13**: 387-392 [PMID: 24790494]
 - 24 **Arifin N**, Abu Osman NA, Wan Abas WA. Intrarater test-retest reliability of static and dynamic stability indexes measurement using the Biodex Stability System during unilateral stance. *J Appl Biomech* 2014; **30**: 300-304 [PMID: 23878204 DOI: 10.1123/jab.2013-0130]
 - 25 **Jose A** Parraca, Pedro R Olivares, Ana Carbonell-Baeza, Virginia A Aparicio, Jose C Adsuar, Narcis Gusi. Test-Retest reliability of Biodex Balance SD on physically active old people. *J Human Sports Exercise* 2011; **6**: 444-450 [DOI: 10.4100/jhse.2011.62.25]
 - 26 **Huxhold O**, Li SC, Schmiedek F, Lindenberger U. Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Res Bull* 2006; **69**: 294-305 [PMID: 16564425 DOI: 10.1016/j.brainresbull.2006.01.002]
 - 27 **O'Shea S**, Morris ME, Iansel R. Dual task interference during gait in people with Parkinson disease: effects of motor versus cognitive secondary tasks. *Phys Ther* 2002; **82**: 888-897 [PMID: 12201803]
 - 28 **Brauer SG**, Morris ME. Can people with Parkinson's disease improve dual tasking when walking? *Gait Posture* 2010; **31**: 229-233 [PMID: 19969461 DOI: 10.1016/j.gaitpost.2009.10.011]
 - 29 **Broglio SP**, Tomporowski PD, Ferrara MS. Balance performance with a cognitive task: a dual-task testing paradigm. *Med Sci Sports Exerc* 2005; **37**: 689-695 [PMID: 15809571 DOI: 10.1249/01.MSS.0000159019.14919.09]
 - 30 **Rahnama L**, Salavati M, Akhbari B, Mazaheri M. Attentional demands and postural control in athletes with and without functional ankle instability. *J Orthop Sports Phys Ther* 2010; **40**: 180-187 [PMID: 20195021 DOI: 10.2519/jospt.2010.3188]
 - 31 **Lamoth CJ**, Stins JF, Pont M, Kerckhoff F, Beek PJ. Effects of attention on the control of locomotion in individuals with chronic low back pain. *J Neuroeng Rehabil* 2008; **5**: 13 [PMID: 18439264 DOI: 10.1186/1743-0003-5-13]
 - 32 **Lauffer Y**, Rotem-Lehrer N, Ronen Z, Khayutin G, Rozenberg I. Effect of attention focus on acquisition and retention of postural control following ankle sprain. *Arch Phys Med Rehabil* 2007; **88**: 105-108 [PMID: 17207684 DOI: 10.1016/j.apmr.2006.10.028]
 - 33 **Riley MA**, Baker AA, Schmit JM. Inverse relation between postural variability and difficulty of a concurrent short-term memory task. *Brain Res Bull* 2003; **62**: 191-195 [PMID: 14698352 DOI: 10.1016/j.brainresbull.2003.09.012]
 - 34 **Salavati M**, Mazaheri M, Negahban H, Ebrahimi I, Jafari AH, Kazemnejad A, Parnianpour M. Effect of dual-tasking on postural control in subjects with nonspecific low back pain. *Spine (Phila Pa 1976)* 2009; **34**: 1415-1421 [PMID: 19478663 DOI: 10.1097/BRS.0b013e3181a3a917]
 - 35 **Pescatello LS**, American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription Ninth Edition: RC684.E9 A37 2014. Philadelphia PA: Wolters Kluwer/Lippincott Williams & Wilkins Health, 2014: 23-24
 - 36 **Holme E**, Magnusson SP, Becher K, Bieler T, Aagaard P, Kjaer M. The effect of supervised rehabilitation on strength, postural sway, position sense and re-injury risk after acute ankle ligament sprain. *Scand J Med Sci Sports* 1999; **9**: 104-109 [PMID: 10220845 DOI: 10.1111/j.1600-0838.1999.tb00217.x]
 - 37 **Gross MT**. Effects of recurrent lateral ankle sprains on active and passive judgements of joint position. *Phys Ther* 1987; **67**: 1505-1509 [PMID: 3659134]
 - 38 **Hiller CE**, Nightingale EJ, Lin CW, Coughlan GF, Caulfield B, Delahunt E. Characteristics of people with recurrent ankle sprains: a systematic review with meta-analysis. *Br J Sports Med* 2011; **45**: 660-672 [PMID: 21257670 DOI: 10.1136/bjsm.2010.077404]

P- Reviewer: Jiao C, Zheng N S- Editor: Ji FF L- Editor: A
E- Editor: Lu YJ



Case Control Study

Benefits of the use of blood conservation in scoliosis surgery

Peter R Loughenbury, Lyeanda Berry, Ben T Brooke, Abhay S Rao, Robert A Dunsmuir, Peter A Millner

Peter R Loughenbury, Lyeanda Berry, Ben T Brooke, Abhay S Rao, Robert A Dunsmuir, Peter A Millner, Department of Neurosciences, Leeds General Infirmary, Leeds LS1 3EX, United Kingdom

Author contributions: Loughenbury PR was involved in study design, data collection, data analysis and wrote the manuscript; Berry L was involved in study design, data collection and review of the manuscript; Brooke BT was involved in data collection and analysis; Rao AS, Dunsmuir RA and Millner PA were involved in study design, data analysis and preparation of the manuscript.

Institutional review board statement: This study was reviewed and approved by the Leeds Teaching Hospitals Institutional Review Board.

Informed consent statement: All study participants, or their legal guardian, provided informed consent prior to study enrolment.

Conflict-of-interest statement: The authors declare that there is no conflict of interest regarding publication of this article.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at p.loughenbury@nhs.net. Consent for data sharing was not obtained but the presented data are anonymized and risk of identification is low.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Peter R Loughenbury, MSc FRCS (Tr and Orth), National Spine Fellow, Department of Neurosciences, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, United Kingdom. p.loughenbury@nhs.net
Telephone: +44-011-32432799

Received: June 11, 2016

Peer-review started: June 17, 2016

First decision: July 29, 2016

Revised: August 9, 2016

Accepted: October 1, 2016

Article in press: October 3, 2016

Published online: December 18, 2016

Abstract

AIM

To investigate whether autologous blood transfusion (ABT) drains and intra-operative cell salvage reduced donor blood transfusion requirements during scoliosis surgery.

METHODS

Retrospective data collection on transfusion requirements of patients undergoing scoliosis surgery is between January 2006 and March 2010. There were three distinct phases of transfusion practice over this time: Group A received "traditional treatment" with allogeneic red cell transfusion (ARCT) in response to an intra- or post-operative anaemia (Hb < 8 g/dL or a symptomatic anaemia); Group B received intra-operative cell salvage in addition to "traditional treatment". In group C, ABT wound drains were used together with both intra-operative cell salvage and "traditional treatment".

RESULTS

Data from 97 procedures on 77 patients, there was no difference in mean preoperative haemoglobin levels between the groups (A: 13.1 g/dL; B: 13.49 g/dL; C: 13.66 g/dL). Allogeneic red cell transfusion was required for 22 of the 37 procedures (59%) in group A, 17 of 30 (57%) in group B and 16 of 30 (53%) in group C. There was an overall 6% reduction in the proportion of patients requiring an ARCT between groups A and C but this was not statistically significant ($\chi^2 = 0.398$). Patients

in group C received fewer units (mean 2.19) than group B (mean 2.94) ($P = 0.984$) and significantly fewer than those in group A (mean 3.82) ($P = 0.0322$). Mean length of inpatient stay was lower in group C (8.65 d) than in groups B (12.83) or A (12.62).

CONCLUSION

When used alongside measures to minimise blood loss during surgery, ABT drains and intra-operative cell salvage leads to a reduced need for donor blood transfusion in patients undergoing scoliosis surgery.

Key words: Blood conservation; Scoliosis; Autologous blood; Cell salvage; Transfusion

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: To our knowledge this is the first report of autologous blood transfusion (ABT) drain use in scoliosis surgery and suggests that its use is both safe and cost effective. When used as part of a systematic programme to minimise blood loss during surgery, the use of ABT drains and intra-operative cell salvage leads to a reduced need for donor blood transfusion in patients undergoing scoliosis surgery.

Loughenbury PR, Berry L, Brooke BT, Rao AS, Dunsmuir RA, Millner PA. Benefits of the use of blood conservation in scoliosis surgery. *World J Orthop* 2016; 7(12): 808-813 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/808.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.808>

INTRODUCTION

Autologous blood reinfusion techniques have become commonplace in many fields of orthopaedic surgery, especially in hip and knee arthroplasty^[1,2]. These techniques can reduce the need for donor blood and the risks that accompany its use, such as incorrect blood component transfused, transfusion reactions, viral/prion disease transmission, and the metabolic and immunological consequences of transfusing allogeneic blood^[3].

The use of autologous blood reinfusion in spinal surgery is less commonly reported. Intra-operative cell salvage has been associated with reduced transfusion requirements in scoliosis surgery^[4,5], but the use of post-operative reinfusion devices is not well documented. Reports are limited to short segment spinal fusion and have not included corrective surgery to treat scoliosis^[6]. This study was designed to determine the effect of sequentially introducing intra-operative cell salvage and post-operative autologous blood transfusion (ABT) drains in scoliosis surgery. These were used alongside a number of efforts to reduce the need for allogeneic red cell transfusion (ARCT) during scoliosis surgery including a

move from two-stage (anterior and posterior) surgery to a single stage (posterior) technique, and measures such as optimisation of pre-surgical haemoglobin levels, oral iron supplements and the antifibrinolytic drug tranexamic acid.

This study aimed: To examine the impact of using ABT drains and intra-operative cell salvage on the allogeneic transfusion requirements for scoliosis surgery in our unit; to evaluate the volume of blood drained and re-transfused using ABT drains.

MATERIALS AND METHODS

This is a retrospective analysis of all patients undergoing surgery for scoliosis in a single centre between January 2006 and March 2010. All patients undergoing corrective scoliosis surgery were included, including revision procedures. Patients under the age of six were excluded, as autologous re-transfusion systems are not recommended for use below this age.

Data was collected from the patient case notes, the transfusion laboratory database and the hospital results server. A data collection form was developed and completed by either the Transfusion Practitioner or Specialist Registrar working in the unit. Patient demographics, details of any preoperative optimisation required, pre- and post-operative haemoglobin levels, donor and autologous transfusion requirements, length of hospital stay and post-operative complications were documented.

The transfusion trigger remained constant across the series. An intra- or post-operative anaemia (Hb < 8 g/dL) or symptomatic anaemia initiated treatment with ARCT. The volume and timing of these transfusions was recorded.

Over this time period there were three distinct phases of transfusion practice: (1) Group A: January to December 2006: "Traditional treatment": These patients received ARCT in response to the transfusion trigger. No autologous blood was transfused ($n = 37$); (2) Group B: January to December 2007. Intra-operative cell salvage was implemented using the Sorin Dideco (Sorin Group, Mirandola, Italy) system ($n = 30$); (3) Group C: January 2008 to March 2010. In addition to intra-operative cell salvage a Bellovac™ (Astra Tech, AB) autologous blood transfusion wound drain was used. Blood collected in the Bellovac™ (Astra Tech) drain was reinfused in accordance with manufacturers guidelines within 6 h of the procedure. The volume of blood collected and reinfused was recorded using the Bellovac™ ABT Management chart provided with the drain ($n = 30$).

Administration of pharmacological agents, such as tranexamic acid, was led by the Consultant Anaesthetist for the case, with no standard guidelines. The doses of any preoperative antifibrinolytics were therefore variable, but were recorded for all patients.

Statistical analysis was carried out using Microsoft Excel. χ^2 tests were used to determine the significance of changes in the proportion of patients requiring an

Table 1 Case mix and patient demographics

Group	n	Median age (range)	Case mix
A	37	15 (8-33)	8 posterior 3 anterior 12 anterior/posterior staged 2 anterior/posterior combined
B	30	16 (9-57)	8 posterior 3 anterior 6 anterior/posterior staged 7 anterior/posterior combined
C	30	15 (11-74)	22 posterior 1 anterior 2 anterior/posterior 3 anterior/posterior combined

ARCT and produce a two-tailed *P* value of significance. Where means are compared a paired *t*-test was used.

RESULTS

Data was collected for 97 procedures on 77 patients between January 2006 and March 2010. Median age of patients was 15 (range 8-74). Group A (January 2006 to December 2006) contained 37 procedures with a median patient age of 15 (range 8-33); group B (January 2007 to December 2007) contained 30 procedures with a median patient age of 16 (range 9-57) and group C (January 2008 to March 2010) contained 30 procedures with a median patient age of 15 (range 11-74). The case mix in each group is detailed in Table 1.

Pre-operative haemoglobin levels

There was no difference in the mean preoperative haemoglobin level. The mean preoperative haemoglobin was 13.09 g/dL (95%CI: 12.60-13.58) in group A, 13.49 g/dL (95%CI: 12.89-14.08) in group B and 13.66 g/dL (95%CI: 13.19-14.13) in group C.

Antifibrinolytics

In group A one patient received a 50 mg dose of tranexamic acid before surgery but no other patients received antifibrinolytic therapy. No patients in group B received antifibrinolytic therapy. In group C, 9 out of 30 patients (30%) were given tranexamic acid before surgery with the dose varying from 350 mg to 1 g. There were no patients in any group taking antiplatelet medication or other agents that would increase bleeding risk.

Volume of autologous blood received

Patients in group A did not receive any autologous blood. Those in group B received intra-operative transfusion of blood collected through the cell saver. The mean volume of blood reinfused was 413.4 mL (SD 287.34 mL). There were technical problems that interrupted reinfusion in 4 out of 30 cases.

Patients in group C received autologous blood from both the cell saver and ABT drains. Intraoperative cell-

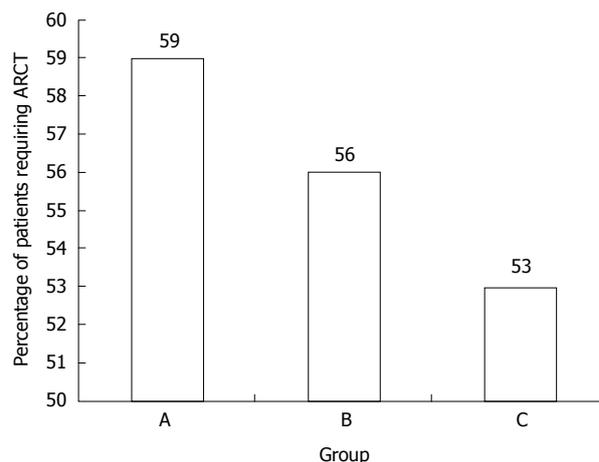


Figure 1 Percentage of patients requiring an allogeneic red cell transfusion. ARCT: Allogeneic red cell transfusion.

salvage was used successfully during 26 out of 30 procedures (87%). Technical problems or insufficient volume collected prevented reinfusion in the remaining four cases. The mean volume of cell saver blood reinfused was 525.4 mL (SD 302.96 mL). ABT drains were used successfully in 28 out of 30 cases. Technical problems and unavailability of equipment prevented reinfusion in the other two cases. The mean volume of blood received through the ABT drain was 442 mL (SD 169.38 mL).

ARCT requirements

A comparison of the ARCT requirements in groups A, B and C is shown in Table 2 and Figures 1 and 2.

There was an overall 6% reduction in the proportion of patients requiring an ARCT between groups A and C (Figure 1) but this was not statistically significant ($\chi^2 = 0.398$). The percentage of patients receiving an ARCT fell from 59% in group A to 56% in group B (not significant; $\chi^2 = 0.068$) and 53% in group C (not significant; $\chi^2 = 0.134$).

In patients requiring allogeneic transfusion, the mean number of units transfused fell from 3.82 units (SD 3.79) in group A to 2.94 (SD 1.82) in group B (not significant; $P = 0.894$) and 2.19 units (SD 0.91) in group C (not significant; $P = 0.0843$). However, the reduction in the mean number of allogeneic units transfused in groups A and C was statistically significant: - 3.82 units in group A to 2.19 units in group C (Figure 2; $P = 0.0322$). There was no difference in ARCT requirements when comparing primary and revision procedures.

A reduction in the length of hospital stay between the groups was also noted. The mean length of stay was 12.62 d (range 8-21) in group A, 12.83 d (range 6-31) in group B and 8.65 d (range 5-23) in group C.

There were no complications relating to allogeneic or autologous transfusion in groups A and B. One patient in group C developed a pyrexia of unknown origin following surgery but this settled without the need for medical intervention. This patient received reinfused blood through the ABT drain but not the cell saver and

Table 2 Allogeneic red cell transfusion requirements

Group	Proportion requiring ARCT	Total number of units received	Mean ARCT (standard deviation)
A	22/37 (59%)	84 (73 units packed red cells, 8 units fresh frozen plasma, 2 units of cryoprecipitate and one unit of platelets)	3.82 units (3.79)
B	17/30 (57%)	50 units packed red cells	2.94 units (1.82)
C	16/30 (53%)	37 units packed red cells	2.19 units (0.91)

ARCT: Allogeneic red cell transfusion.

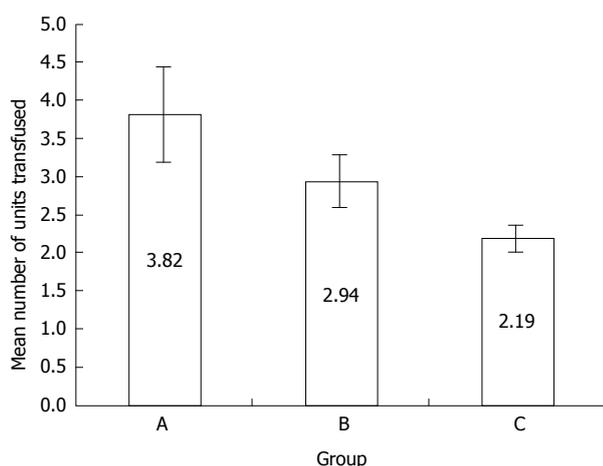


Figure 2 Mean number of units transfused.

did not receive any allogeneic blood. There were no other complications in group C.

DISCUSSION

As part of an integrated blood conservation programme, autologous blood reinfusion can reduce the need for, and the potential complications of, donor blood transfusion. These include transfusion of incorrect blood components, transfusion reactions, viral/prion disease transmission, coagulopathy, and the metabolic and immunological consequences of transfusing allogeneic blood^[3].

Autologous blood reinfusion in the form of cell salvage has become commonplace in many fields of orthopaedic surgery^[1,2]. Its use in other adult elective orthopaedic procedures has been shown to reduce the rate of exposure to allogeneic red cell transfusion (RR = 0.42; 95%CI: 0.32-0.54)^[7]. In adult spinal surgery, transfusion requirements in both elective surgery and operative fracture fixation are significantly lower when cell salvage is used^[1]. The benefits of cell salvage in scoliosis surgery are less clear, but have been reported in both posterior and anterior scoliosis surgery^[4,8]. In their retrospective case-controlled study of 137 consecutive patients, Mirza *et al*^[8] underlined the benefits of cell salvage in instrumented anterior scoliosis surgery. The need for allogeneic blood fell from 39.4% in the control group ($n = 33$) to 6.7% in the study group ($n = 104$) ($P < 0.0001$). Bowen *et al*^[4] reported a retrospective case control study in which the routine use of the cell saver during posterior

spinal fusion for paediatric idiopathic scoliosis, was associated with decreased allogeneic transfusion rates, particularly for procedures lasting over 6 h and where expected blood loss was over 30% of blood volume.

The use of ABT drains has also become more popular in orthopaedic procedures over the last ten years. Post-operative collection and reinfusion of red cells has been shown to reduce the need for donor blood transfusion in both knee and hip arthroplasty^[9,10]. In spinal surgery, re-transfusion drains have been shown to be safe and reduce the need for donor blood during short segment fusion in adults^[6]. The use of ABT drains in scoliosis surgery has not previously been reported.

In our study both cell salvage and ABT drains were sequentially introduced and lead to a modest, but not statistically significant, reduction in the percentage of patients receiving an allogeneic transfusion. However, those patients who were transfused were exposed to significantly fewer allogeneic units (donor exposures), falling from 3.82 to 2.19 units when both intraoperative cell salvage and ABT drains were used.

In common with all retrospective studies, it is impossible to adjust for all confounders, both known and unknown. The reduction in donor blood exposure we achieved occurred alongside a number of other changes to minimise blood loss during surgery during the study period. There was a trend towards less invasive surgical procedures in groups B and C, partly due to changes in the implant systems used which provided a greater ability to achieve an adequate curve correction using a single stage posterior procedure. There was also a trend towards an increased use of antifibrinolytics in group C (30% of whom received tranexamic acid), and there is good evidence that this can lead to lower transfusion rates in paediatric scoliosis surgery^[11].

In the absence of randomised controlled trials, the results of retrospective series, such as this, must be interpreted with caution. However, the methods described were found to be safe and practical in routine practice and contributed to a clinically and financially worthwhile reduction in the use of donor red cells.

We also observed a fall in the length of inpatient hospital stay in patients in group C. This is probably multifactorial, including changes to surgical practice that lead to earlier postoperative mobilisation and discharge. However, changes in transfusion practice may have contributed as several previous studies have reported reduced length of hospital stay in orthopaedic patients

Table 3 Cost analysis comparing groups A, B and C

	Group A donor blood only	Group B cell salvage	Group C cell salvage + ABT drain
Number of RBC units transfused	84	50	37
Total cost of RBC transfusion (£)	10416	6200	4588
Number of patients receiving cell salvage	0	30	30
Total cost of cell Salvage (£)	0	2100	2100
Number of patients receiving ABT drains	0	0	30
Total cost of ABT drains (£)	0	0	1620
Overall transfusion cost	10416	8300	8308
Number of patients	37	30	30
Overall cost per patient (£)	281.51	276.67	276.93

RBC = £124; cost of cell salvage ACD-A, collection and processing kit = £70; costs of a single ABT drain = £54. ABT: Autologous blood transfusion; RBC: Cost of one unit of blood; ACD-A: Acid citrate-dextrose anticoagulant.

exposed to less donor blood^[12].

Cost analysis

There is good evidence to suggest that cell salvage is a cost effective method to reduce the need for donor blood transfusion^[13]. A cost analysis of the data presented in our study is detailed in Table 3. This confirms that the use of cell salvage alone and the use of cell salvage with ABT drains was cost neutral in our study.

In conclusion, to our knowledge this is the first report of ABT drain use in scoliosis surgery and suggests that its use is both safe and cost effective. When used as part of a systematic programme to minimise blood loss during surgery, the use of ABT drains and intra-operative cell salvage lead to a reduced need for donor blood transfusion in patients undergoing scoliosis surgery in our unit. The lowest donor blood transfusion rates were seen when both modalities were used, leading to a 6% reduction in the number of donor transfusion episodes and a significant reduction in the mean units of red cells transfused per episode (2.19 compared to 3.82). The programme proved practical and cost-effective to implement in a busy surgical unit.

COMMENTS

Background

Autologous blood reinfusion techniques have become commonplace in many fields of orthopaedic surgery, especially in hip and knee arthroplasty. These techniques can reduce the need for donor blood and the risks that accompany its use.

Research frontiers

Intra-operative cell salvage has been associated with reduced transfusion requirements in scoliosis surgery, but the use of post-operative reinfusion devices is not well documented.

Innovations and breakthroughs

To the authors' knowledge this is the first report of autologous blood transfusion (ABT) drain use in scoliosis surgery and suggests that its use is both safe and cost effective.

Applications

When used as part of a systematic programme to minimise blood loss during

surgery, the use of ABT drains and intra-operative cell salvage can reduce the need for donor blood transfusion in patients undergoing scoliosis surgery.

Terminology

ABT and allogeneic red cell transfusion.

Peer-review

This is a case control study reporting the use of ABT drains in scoliosis surgery and suggests that its use is both safe and cost effective. When used as part of a systematic programme to minimise blood loss during surgery, ABT drains and intra-operative cell salvage lead to a significantly reduced need for donor blood transfusion in patients undergoing scoliosis surgery.

REFERENCES

- Goulet JA**, Bray TJ, Timmerman LA, Benson DR, Bargar WL. Intraoperative autologous transfusion in orthopaedic patients. *J Bone Joint Surg Am* 1989; **71**: 3-8 [PMID: 2913000]
- Huët C**, Salmi LR, Fergusson D, Koopman-van Gemert AW, Rubens F, Laupacis A. A meta-analysis of the effectiveness of cell salvage to minimize perioperative allogeneic blood transfusion in cardiac and orthopedic surgery. International Study of Perioperative Transfusion (ISPT) Investigators. *Anesth Analg* 1999; **89**: 861-869 [PMID: 10512256 DOI: 10.1213/00000539-199910000-00009]
- Bolton-Maggs PH**. Conference report: the 2015 SHOT symposium and report--what's new? *Transfus Med* 2015; **25**: 295-298 [PMID: 26498582 DOI: 10.1111/tme.12257]
- Bowen RE**, Gardner S, Scaduto AA, Eagan M, Beckstead J. Efficacy of intraoperative cell salvage systems in pediatric idiopathic scoliosis patients undergoing posterior spinal fusion with segmental spinal instrumentation. *Spine (Phila Pa 1976)* 2010; **35**: 246-251 [PMID: 20081521 DOI: 10.1097/BRS.0b013e3181bdf22a]
- Weiss JM**, Skaggs D, Tanner J, Tolo V. Cell Saver: is it beneficial in scoliosis surgery? *J Child Orthop* 2007; **1**: 221-227 [PMID: 19308514 DOI: 10.1007/s11832-007-0032-6]
- Sebastián C**, Romero R, Olalla E, Ferrer C, García-Vallejo JJ, Muñoz M. Postoperative blood salvage and reinfusion in spinal surgery: blood quality, effectiveness and impact on patient blood parameters. *Eur Spine J* 2000; **9**: 458-465 [PMID: 11189913 DOI: 10.1007/s005860000167]
- Carless PA**, Henry DA, Moxey AJ, O'Connell DL, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev* 2003; **(4)**: CD001888 [PMID: 14583940 DOI: 10.1002/14651858.cd001888.pub2]
- Mirza AH**, Aldlyami E, Bhimarasetty C, Thompson AG, Spilsbury J, Marks DS. The role of peri-operative cell salvage in instrumented anterior correction of thoracolumbar scoliosis: a case-controlled study. *Acta Orthop Belg* 2009; **75**: 87-93 [PMID: 19358405]
- Peter VK**, Radford M, Matthews MG. Re-transfusion of autologous blood from wound drains: the means for reducing transfusion

- requirements in total knee arthroplasty. *Knee* 2001; **8**: 321-323 [PMID: 11706696 DOI: 10.1016/S0968-0160(01)00122-3]
- 10 **Smith LK**, Williams DH, Langkamer VG. Post-operative blood salvage with autologous retransfusion in primary total hip replacement. *J Bone Joint Surg Br* 2007; **89**: 1092-1097 [PMID: 17785752 DOI: 10.1302/0301-620X.89B8.18736]
- 11 **Grant JA**, Howard J, Luntley J, Harder J, Aleissa S, Parsons D. Perioperative blood transfusion requirements in pediatric scoliosis surgery: the efficacy of tranexamic acid. *J Pediatr Orthop* 2009; **29**: 300-304 [PMID: 19305284 DOI: 10.1097/BPO.0b013e31819a85de]
- 12 **Jans O**, Kehlet H, Hussain Z, Johansson PI. Transfusion practice in hip arthroplasty--a nationwide study. *Vox Sang* 2011; **100**: 374-380 [PMID: 21029109 DOI: 10.1111/j.1423-0410.2010.01428.x]
- 13 **Haynes S**, Payne K, Elliott RA, McCollum C. Cost-effectiveness of cell salvage and alternative methods of minimising perioperative allogeneic blood transfusion: a systematic review and economic model. In: Davies L, Brown TJ, editors. Winchester, England: Health Technology Assessment, 2006: iii-iv, ix-x, 1-210

P- Reviewer: Erkan S, Luo XH, Jain A **S- Editor:** Qiu S
L- Editor: A **E- Editor:** Lu YJ



Retrospective Study

Windsurfing vs kitesurfing: Injuries at the North Sea over a 2-year period

Christiaan JA van Bergen, Joris P Commandeur, Rik IK Weber, Daniel Haverkamp, Roelf S Breederveld

Christiaan JA van Bergen, Department of Orthopaedic Surgery, Spaarne Gasthuis, 2134 TM Hoofddorp, The Netherlands

Joris P Commandeur, Department of Surgery, Luzerner Kantonsspital, 6000 Luzern, Switzerland

Rik IK Weber, Daniel Haverkamp, Department of Orthopaedic Surgery, Slotervaartziekenhuis, 1066 EC Amsterdam, The Netherlands

Roelf S Breederveld, Department of Trauma Surgery, Red Cross Hospital, 1942 LE Beverwijk, The Netherlands

Author contributions: van Bergen CJA designed and performed the study and wrote the article; Commandeur JP helped perform the study; Weber RIK and Haverkamp D assisted in the analysis; Breederveld RS supervised the study; all authors reviewed and commented on the text and approved the final version.

Institutional review board statement: The study was reviewed and approved by the METC Noord-Holland Institutional Review Board.

Informed consent statement: All study participants provided informed consent prior to study enrolment.

Conflict-of-interest statement: The authors have no conflict of interest to report.

Data sharing statement: The anonymized dataset is available from the corresponding author at c.j.vanbergen@amc.nl.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Christiaan JA van Bergen, MD, PhD, Orthopaedic Surgeon, Department of Orthopaedic Surgery, Spaarne Gasthuis, Spaarnepoort 1, 2134 TM Hoofddorp, The Netherlands. c.j.vanbergen@amc.nl
Telephone: +31-23-2240000
Fax: +31-20-5669117

Received: March 27, 2016
Peer-review started: March 30, 2016
First decision: May 13, 2016
Revised: September 26, 2016
Accepted: October 17, 2016
Article in press: October 19, 2016
Published online: December 18, 2016

Abstract

AIM

To analyze all windsurfing and kitesurfing (kiteboarding) injuries presented at our coastal hospital over a 2-year period.

METHODS

Twenty-five windsurfers (21 male; aged 31 ± 8 years) and 32 kitesurfers (23 male; aged 29 ± 11 years) presented at our hospital during the 2-year study period. Various injury data were recorded, including transport to hospital and treatment. After a median follow-up of 16 mo (range, 7-33 mo), 18 windsurfers (72%) and 26 kitesurfers (81%) completed questionnaires on the trauma mechanisms, the use of protective gear, time spent on windsurfing or kitesurfing, time to return to sports, additional injuries, and chronic disability.

RESULTS

Most patients sustained minor injuries but severe injuries also occurred, including vertebral and tibial plateau fractures. The lower extremities were affected the most, followed by the head and cervical spine, the upper

extremities, and the trunk. The injury rates were 5.2 per 1000 h of windsurfing and 7.0 per 1000 h of kitesurfing ($P = 0.005$). The injury severity was the same between groups ($P = 1.0$). Less than 30% of the study population used protective gear. Kitesurfers had a higher number of injuries, and required transport by ambulance, inpatient hospital stay and operative treatment more often than windsurfers, but these differences were not statistically significant ($P > 0.05$). The median time to return to windsurfing and kitesurfing was 5 and 4 wk, respectively ($P = 0.79$). Approximately one-third of the patients in each group experienced chronic symptoms.

CONCLUSION

Kitesurfing results in a significantly higher injury rate than windsurfing in the same environmental conditions but the severity of the injuries does not differ.

Key words: General sports trauma; Extreme sports; Surfing; Epidemiology; Prevention

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: To our knowledge, this is the first study that directly compares kitesurfing and windsurfing in the same weather and environmental conditions, giving a unique insight in the injuries associated with these sports. Kitesurfing resulted in a significantly higher injury rate than windsurfing in the same environmental conditions but the severity of the injuries did not differ. The presented results may assist the health-care professional and the athlete in taking measures to prevent injuries and in advising or choosing the safer sport.

van Bergen CJA, Commandeur JP, Weber RIK, Haverkamp D, Breederveld RS. Windsurfing vs kitesurfing: Injuries at the North Sea over a 2-year period. *World J Orthop* 2016; 7(12): 814-820 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/814.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.814>

INTRODUCTION

Windsurfing has a long history as a popular water sport since its introduction in 1971. It has been recognized as an Olympic sport since 1984. Various reports on windsurfing injuries have been published since 1988^[1-6]. Due to the technical developments, lighter and more sophisticated material, windsurfers have more possibilities to push out their frontiers, possibly exposing them to more dangerous situations (Figure 1).

Kitesurfing (or kiteboarding) is possibly the fastest growing water sport today. Using a small board and a kite of up to 20 m², surfers can achieve huge jumps and great speeds up to 55 knots (Figure 2). This extreme sport has been increasingly popular since it was developed in the late 1990s. In 2006, the total number



Figure 1 Windsurf action.



Figure 2 Kitesurf action.

of kitesurfers worldwide was estimated at around 210000, with 114465 inflatable kites sold that same year according to an in-depth worldwide industry survey^[7]. By 2008, the participation rate growth was between 35% and 50%^[7]. Despite the increasing popularity and possible dangers of this sport, little is known about injury prevalence or prevention^[8]. However, some reports did analyse kitesurfing injuries and even reported fatal accidents^[9-12].

Windsurfing and kitesurfing are sports that have many fundamentals in common; wind is used to generate forward motion on the water, opening the possibility of performing tricks both on the water and in the air. However, the equipment used for these sports are completely different. Windsurfers use a sail with a mast directly connected to the board, whereas kitesurfers use a kite, which is attached to the athlete by multiple lines. Because of these differences, rates and severity of injuries may differ. Interestingly, these sports have never been compared in one study or in the same weather and environmental conditions. Providing comparative data may assist the athlete in taking measures to prevent injuries and in choosing the safer sport.

The aim of this study was to analyze and compare all kitesurfing and windsurfing injuries at our hospital over a 2-year period. We hypothesized that kitesurfing results in more frequent and more severe injuries than windsurfing.



Figure 3 Picture of the popular spot at the North Sea on a typical day, showing windsurfers and kitesurfers mixed.

MATERIALS AND METHODS

This is a retrospective study carried out according to a study protocol approved by the local medical ethics committee. All patients with windsurfing or kitesurfing injuries who presented at our hospital from September 2009 through September 2011 were included. September 2009 was chosen as the starting point of the study since our hospital then introduced the Electronic Patient Data (EPD) system, allowing for reliable inclusion of patients by search criteria.

A place at the North Sea close to our hospital is probably the most popular and most visited kitesurfing and windsurfing location of The Netherlands (Figure 3). Wind speeds are ≥ 4 Beaufort most of the days (60%-70%), and there are waves of up to 4 m. Injured individuals from this place typically present at the Emergency Department of our hospital because it is very close, between the beach and the highway.

Patient identification

The EPD was searched for windsurfing and kitesurfing injuries using the terms "surf" and "kite" with any possible prefix or extension. Thus, each patient with any of these terms - also as part of another word - mentioned in the patient charts was identified.

Data collection

Each patient's chart was manually reviewed. Numerous patient data were recorded, including gender, date of birth, injury data [trauma mechanism, type of injury, affected body part(s)], site of injury (beach or water), transport to hospital, type of treatment, submission to hospital, or outpatient treatment.

Additionally, the patients were sent questionnaires with prepaid envelopes, accompanied by an information letter, containing the following items: (1) skill level (beginner, intermediate, advanced, expert); (2) number of years of experience; participant hours (number of days a year and mean number of hours a day); (3) cause of the injury; wind speed; (4) use of protective gear (helmet, vest) at the time of injury; (5) availability and use of a quick-release system (kitesurfing only);

(6) time to return to windsurfing or kitesurfing; (7) additional injuries during the study period; and (8) chronic symptoms.

For windsurfing, the skill level was assessed by the study participants according to the following scale: Beginner, learning to windsurf, basic tacking and gybing; intermediate, basic beach starting, planing techniques, use of foot straps and harness; advanced, water starting, carve gybe, launching and landing in waves; expert, advances aerial and freestyle manoeuvres^[1]. For kitesurfing, the skill level was assessed by the study participants according to the following scale: Beginner, starting and landing the kite with help, downwind rides on the water; intermediate, easy manoeuvres such as jibes, upwind rides, and small jumps; advanced, high jumps and transition jumps; expert, high jumps with rotation and board-off jumps^[9].

The questionnaire included any information that could not be retrieved from the charts for that specific patient.

The severity of the injury was classified as follows^[9]: (1) catastrophic, injuries leading to permanent disability or death; (2) severe, injuries resulting in absence from kitesurfing or windsurfing for more than 6 wk; (3) medium, injuries resulting in absence from kitesurfing or windsurfing for more than 1 d; and (4) mild, injuries resulting in incapacity to train or compete on a normal basis.

Statistical analysis

Data with a normal distribution are presented as mean \pm standard deviation. Data with a skewed distribution are presented as median and range. Injury rates were calculated per 1000 h of windsurfing or kitesurfing. Various data were compared between windsurfing and kitesurfing with use of parametric or nonparametric statistical tests, depending on the number and distribution of data (Student *t*-test for age; Mann-Whitney *U* test for other continuous data; χ^2 or Fisher's Exact test for nominal and categorical data, where appropriate). A *P*-value of 0.05 was considered to be statistically significant.

RESULTS

The computer-generated search and manual chart review identified 57 patients (25 windsurfers and 32 kitesurfers) who had presented at our Emergency Department during the study period.

Baseline characteristics and protective gear

There were 44 male and 13 female patients with a mean age of 30 ± 10 (range, 11-57) years. Eighteen windsurfers (72%) and 26 kitesurfers (81%) completed the questionnaire. The median time to follow-up was 16 mo (range, 7-33 mo). Most baseline characteristics were not significantly different between the groups, but windsurfers had significantly more experience and

Table 1 Baseline characteristics

	Windsurfing	Kitesurfing	P-value
Age (yr)	31 ± 8	29 ± 11	0.437
Gender (No. and % of patients)			0.279
Male	21 (84%)	23 (72%)	
Female	4 (16%)	9 (28%)	
Experience (yr)	15 (0-30)	2 (0-12)	< 0.001
Annual participant hours	106 (1-480)	70 (1-810)	0.184
Skills level			0.001
Beginner	1 (4%)	11 (34%)	
Intermediate	0 (0%)	6 (19%)	
Advanced	9 (36%)	3 (9%)	
Expert	8 (32%)	6 (19%)	
Wind speed (Bft)	6 (2-8.5)	5 (2-9)	0.362
Protective gear (No. and % of patients)	3 (17%)	7 (28%)	0.480

Data are presented as mean ± standard deviation in case of normal distribution, and as median (range) in case of skewed distribution.

a higher skills level than kitesurfers (Table 1). Only 17% in the windsurf group and 28% in the kitesurf group used protective gear such as helmets and body protectors (impact vests). A quick-release system was present in 24 (92%) out of 26 kitesurfers, but it was deployed by only eight (31%).

Injury rates

In the windsurf group, 32 injuries occurred during a total of 6146 windsurfing hours during the study period of 2 years. This corresponds with an overall injury rate of 5.2 injuries per 1000 h of windsurfing (Table 2). In the kitesurf group, 49 injuries occurred during a total of 6978 kitesurfing hours in 2 years, which corresponds with an overall injury rate of 7.0 injuries per 1000 h of kitesurfing. The difference between the groups was statistically significant ($P = 0.005$).

Injury patterns and severity

In the windsurf group, most injuries generally occurred during difficult manoeuvres such as forward and back loops, or due to unexpected wind gusts. Likewise, in the kitesurf group most injuries were caused by high jumps or wind gusts; additionally, many of the injuries in this group were caused by technical difficulties controlling the kite and/or board. Only few injuries in both groups were the result of collisions with other surfers.

Most patients in both groups sustained minor injuries, such as contusions, lacerations, and ankle sprains. However, numerous serious injuries also occurred. In the windsurf group, serious injuries included fractures of the tibial plateau and os trapezium. In the kitesurf group, there were fractures of the dens, L3 vertebral body, olecranon, scaphoid, tibial plateau, and talus. The lower extremities were affected the most, followed by the head and cervical spine, the upper extremities, and the trunk, respectively (Table 2).

The severity of the injuries was graded as medium or severe in most cases of both groups (Table 2).

Table 2 Injury data

	Windsurfing	Kitesurfing	P-value
Number of injuries per 1000 h	5.2	7	0.005
Affected body site (No. and % of patients)			0.413
Head and cervical spine	9 (36%)	11 (34%)	
Upper extremity	6 (24%)	5 (16%)	
Trunk and thoracolumbar spine	0 (0%)	3 (9%)	
Lower extremity	10 (40%)	13 (41%)	
Injury severity (No. and % of patients)			1.000
Mild	3 (17%)	5 (19%)	
Medium	6 (33%)	9 (35%)	
Severe	8 (44%)	10 (39%)	
Catastrophic	1 (6%)	2 (8%)	
Location of accident (No. and % of patients)			0.014
Water	17 (94%)	15 (58%)	
Beach	1 (6%)	11 (42%)	
Type of transport (No. and % of patients)			0.161
Ambulance	2 (11%)	8 (31%)	
Own transport	16 (89%)	18 (69%)	
Inpatient hospital stay (No. and % of patients)	1 (4%)	5 (16%)	0.215
Operative treatment (No. and % of patients)	1 (4%)	4 (13%)	0.372
Total number of injuries during study period (No. and % of patients)			0.237
1	20 (80%)	19 (59%)	
2	3 (12%)	9 (28%)	
3	2 (8%)	4 (13%)	
Return to sports in weeks (median and range)	5 (0-chronic)	4 (0-chronic)	0.792
Chronic symptoms (No. and % of patients)	7 (39%)	8 (31%)	0.576

The injury severity was neither significantly different between the groups, nor associated with patient age, skills level, or the use of protective gear.

Although kitesurfers had a higher number of injuries and required transport by ambulance, inpatient hospital stay and operative treatment more frequently than windsurfers, these differences were not statistically significant (Table 2). Kitesurfing accidents happened significantly more on the beach than windsurfing accidents ($P = 0.014$).

The median time to return to sports was approximately 1 mo (Table 2). About one-third of the patients experienced chronic symptoms due to the accident at the time of follow-up (Table 2).

DISCUSSION

Windsurfing and kitesurfing are sports that are closely connected to the elements. As such, these sports have a certain level of unpredictability. These properties might be the reasons why these sports are so popular. However, the unpredictability might also impose a key factor in the risks associated with these sports. Therefore, finding typical trauma mechanisms and

handles for prevention is challenging.

Injury rates

The main objective of this study was to investigate the incidence of injuries among both windsurfers and kitesurfers and thus generate an objective image of the risk incorporated in these sports. The results suggest that kitesurfing has a significantly higher injury rate than windsurfing. We found an injury rate of 5.2 per 1000 h of windsurfing compared to 7.0 injuries per 1000 h of kitesurfing.

The groups were comparable with regard to age, gender, weather conditions, and participant hours. However, the average experience and skills level were higher amongst windsurfers. One might speculate that less experienced athletes sustain more severe injuries, which could partially explain the outcomes of our study. However, another study found that having more experience increases the risk of significant injuries among recreational surfers^[13]. Therefore, the explanation for the different injury rates between the groups in our study might be found in the technical differences between sports and in the risks associated with the gear used, rather than the experience of the sportsmen.

In the literature, a few previous studies reported injury rates. A review of the literature identified an overall injury rate of 5.9 to 7.0 injuries per 1000 noncompetitive kitesurfing hours^[12]. A prospective kitesurf study showed an injury rate of 7 injuries per 1000 h of practicing the sport^[9]. This rate is the same as that found for kitesurfing in our retrospective study. For windsurfing, however, lower injury rates have been reported in retrospective studies. McCormick *et al*^[4] in 1988 found an injury rate of 0.22 injuries per 1000 h of practicing windsurfing. Other reported injury rates in windsurfing ranged from 1.1 to 2.0 injuries/person per year^[1,6]. These rates are somewhat lower than ours. Possible interpretations for these differences might be found in the different weather and water conditions between studies and in an evolution of the sport since 1988, possibly adding more risk. Furthermore, the rates found in our study might be overestimated because only injured individuals were included.

Both windsurfing and kitesurfing clearly have lower injury rates compared with other extreme sports and contact sports. For example, American football, motocross, and football (soccer) have injury rates of 36, 23, and 19 per 1000 h, respectively^[14-16]. However, conclusions from comparing injury rates between different studies should be interpreted with caution due to the lack of a uniform injury definition in sports science.

Injury patterns and severity

We found no difference in injury severity between the kitesurf and windsurf groups. In both groups, the majority of injuries were relatively minor, with the highest prevalence in the lower extremities. Previous studies

showed comparable patterns, severity and location of injuries^[1,9,11]. The injury severity was not associated with patient age, skills level or the use of protective gear. However, the study may not have enough numbers in the subgroups to support this with confidence (causing a statistic error type II).

In windsurfing, the most common causes of injuries were technical manoeuvres and unexpected wind gusts. The leading causes of injuries in kitesurfing were jumps, wind gusts and lack of controlling the kite. These findings concur with other studies^[9,11]. The fact that kitesurfers lost control more often might be due to less experience, a difference in the technical aspects of controlling a kite, or a larger surface of a kite than a windsurf sail.

Dyson *et al*^[1] reported collision with equipment to be the major contributor to injuries of windsurfers. Nickel *et al*^[9] suggested separating designated areas for windsurfers and kitesurfers to prevent collisions. However, in our study that addressed both sports, collisions were reported infrequently. According to these results, separation of windsurfing and kitesurfing areas seems unnecessary.

Injury prevention

Little is known about the effect of protective gear in the prevention of windsurf and kitesurf related injuries. The equipment of both sports has evolved during the past decades. In windsurfing, the changes have been subtle. Booms are smaller and foot straps are designed for easier exit. Given the fact that kitesurfing is a relatively young sport, equipment evolution is most notable in this sport; the major advancement being a quick-release safety system, enabling kitesurfers to release the kite easily in case of emergency (Figure 4). Although most kitesurfers had a quick-release system on their kite, the minority deployed it. The use of protective gear such as helmets, impact vests and flotation devices has been accepted more and more. However, only still a small percentage of the athletes use protective equipment, as is shown in our study as well as previous studies^[8,11]. Better use of quick-release systems and protective gear offers possibilities for education and counseling.

In kitesurfing, significantly more accidents occurred on the beach (42% vs 6% for windsurfing). Launching and landing the kite on the beach are the times that kitesurfers are classically at risk, particularly if inexperienced, as an accident at this time means the kiter lands on a hard surface (beach) as opposed to water. These data provide another handle for prevention, with focus on education and awareness regarding the risk of injury during launching and landing the kite.

Other sources of injury prevention are exercises and warming up. Dyson *et al*^[1] reported a relatively high incidence of lower back problems amongst windsurfers and stated a possible role for back exercises in the prevention of these injuries. Lundgren *et al*^[17] found a protective effect of a warming-up before starting a



Figure 4 Picture showing (1) the kite, (2) the handlebar, and (3) the quick-release system.

kitesurf session.

Limitations

The identification of study patients through searching the EPD might not have detected patients in case the words “surf” or “kite” were not used in the patient’s file. The injury rates in this study were calculated retrospectively. It might be difficult for participants to estimate the hours they practiced sports during the time period of the study, although any uncertainty would affect both groups. Furthermore, only athletes who presented at our hospital were included. It might be conceivable that these windsurfers and kitesurfers are more prone to injuries than others. The total amount of windsurfers and kitesurfers is unknown. These factors might result in injury rates that are reported higher than they actually are. However, the results for kitesurfers are the same as those found in a prospective study^[9], which might support the validity of our findings. Lastly, the group sizes in our study were limited. This may partially explain the fact that differences between groups concerning transport by ambulance, inpatient hospital stay and operative treatment did not reach statistical significance. Future studies following large groups of surfers prospectively throughout multiple seasons may provide the most reliable data to analyse and compare injuries.

In conclusion, to our knowledge, this is the first study that directly compares kitesurfing and windsurfing in the same conditions, giving a unique insight in the injuries associated with these sports during a 2-year period. The outcomes suggest that kitesurfing has a higher injury rate than windsurfing. The severity of injuries was similar.

COMMENTS

Background

Windsurfing has been a popular water sport for over three decades. Kitesurfing is possibly the fastest growing water sport today. Windsurfing and kitesurfing are sports that have many fundamentals in common; wind is used to generate forward motion on the water, opening the possibility of performing tricks both on the water and in the air. Thus, both extreme sports pose the athlete at risk for

injuries. However, the equipment used for these sports are completely different. Windsurfers use a sail with a mast directly connected to the board, whereas kitesurfers use a kite, which is attached to the athlete by multiple lines. Because of these differences, rates and severity of injuries may differ.

Research frontiers

Various reports on windsurfing injuries have been published since 1988. Some other reports have analysed kitesurfing injuries and even reported fatal accidents. Current research aims to further identify trauma mechanisms and provide handles for prevention.

Innovations and breakthroughs

To the authors’ knowledge, this is the first study that directly compares kitesurfing and windsurfing in the same conditions, giving a unique insight in the injuries associated with these sports during a 2-year period. The outcomes suggest that kitesurfing has a higher injury rate than windsurfing. Injury data are presented and preventive measures are suggested.

Applications

The provided comparative data may assist the athlete and sport physician in taking measures to prevent injuries and in choosing the safer sport. This study forms a base for future research investigating larger groups of surfers prospectively to provide the most reliable data on injuries.

Peer-review

It is an interesting manuscript on investigating and comparing windsurf vs kite surf in the same conditions giving a description of the associated injuries. Overall the structure of the manuscript is very good and the language of the manuscript reaches the standard of publishing.

REFERENCES

- 1 **Dyson R**, Buchanan M, Hale T. Incidence of sports injuries in elite competitive and recreational windsurfers. *Br J Sports Med* 2006; **40**: 346-350 [PMID: 16556791 DOI: 10.1136/bjism.2005.023077]
- 2 **Gosheger G**, Jägersberg K, Linnenbecker S, Meissner HJ, Winkelmann W. [Injury patterns and prevention in World Cup windsurfing]. *Sportverletz Sportschaden* 2001; **15**: 50-54 [PMID: 11475622 DOI: 10.1055/s-2001-14815]
- 3 **Kalogeromitros A**, Tsangaris H, Bilalis D, Karabinis A. Severe accidents due to windsurfing in the Aegean Sea. *Eur J Emerg Med* 2002; **9**: 149-154 [PMID: 12131638 DOI: 10.1097/00063110-200206000-00009]
- 4 **McCormick DP**, Davis AL. Injuries in sailboard enthusiasts. *Br J Sports Med* 1988; **22**: 95-97 [PMID: 3233460 DOI: 10.1136/bjism.22.3.95]
- 5 **Nathanson AT**, Reinert SE. Windsurfing injuries: results of a paper- and Internet-based survey. *Wilderness Environ Med* 1999; **10**: 218-225 [PMID: 10628281]
- 6 **Neville V**, Folland JP. The epidemiology and aetiology of injuries in sailing. *Sports Med* 2009; **39**: 129-145 [PMID: 19203134 DOI: 10.2165/00007256-200939020-00003]
- 7 Kiteboarding Statistics: Worldwide Participation and Sales Figures. Available from: URL: http://www.sbckiteboard.com/search_article?news_id=418
- 8 **Exadaktylos AK**, Scwabas GM, Blake I, Swemmer K, McCormick G, Erasmus P. The kick with the kite: an analysis of kite surfing related off shore rescue missions in Cape Town, South Africa. *Br J Sports Med* 2005; **39**: e26; discussion e26 [PMID: 15849279 DOI: 10.1136/bjism.2004.014795]
- 9 **Nickel C**, Zernial O, Musahl V, Hansen U, Zantop T, Petersen W. A prospective study of kitesurfing injuries. *Am J Sports Med* 2004; **32**: 921-927 [PMID: 15150038 DOI: 10.1177/0363546503262162]
- 10 **Scheibe E**, Lignitz E, Hinz P, Scheibe R. [Kitesurfing. A new trend sport but not without danger.]. *Rechtsmedizin* 2009; **19**: 145-151 [DOI: 10.1007/s00194-009-0597-0]
- 11 **Spanjersberg WR**, Schipper IB. Kitesurfing: when fun turns to trauma-the dangers of a new extreme sport. *J Trauma* 2007; **63**:

- E76-E80 [PMID: 17554218 DOI: 10.1097/TA.0b013e318046edfd]
- 12 **Bourgeois JG**, Boone J, Callewaert M, Tipton MJ, Tallir IB. Biomechanical and physiological demands of kitesurfing and epidemiology of injury among kitesurfers. *Sports Med* 2014; **44**: 55-66 [PMID: 24105613 DOI: 10.1007/s40279-013-0103-4]
 - 13 **Pikora TJ**, Braham R, Mills C. The epidemiology of injury among surfers, kite surfers and personal watercraft riders: wind and waves. *Med Sport Sci* 2012; **58**: 80-97 [PMID: 22824840 DOI: 10.1159/000338583]
 - 14 **Dick R**, Ferrara MS, Agel J, Courson R, Marshall SW, Hanley MJ, Reifsteck F. Descriptive epidemiology of collegiate men's football injuries: National Collegiate Athletic Association Injury Surveillance System, 1988-1989 through 2003-2004. *J Athl Train* 2007; **42**: 221-233 [PMID: 17710170]
 - 15 **Gobbi A**, Tuy B, Panuncialman I. The incidence of motocross injuries: a 12-year investigation. *Knee Surg Sports Traumatol Arthrosc* 2004; **12**: 574-580 [PMID: 15133584 DOI: 10.1007/s00167-004-0510-z]
 - 16 **Nielsen AB**, Yde J. Epidemiology and traumatology of injuries in soccer. *Am J Sports Med* 1989; **17**: 803-807 [PMID: 2516415 DOI: 10.1177/036354658901700614]
 - 17 **Lundgren L**, Brorsson S, Osvalder AL. Comfort aspects important for the performance and safety of kitesurfing. *Work* 2012; **41** Suppl 1: 1221-1225 [PMID: 22316886]

P- Reviewer: Angoules A, Drampalos E, Hernandez-Sanchez S
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Lu YJ



Retrospective Study

Seasonal variation in adult hip disease secondary to osteoarthritis and developmental dysplasia of the hip

Tatsuya Sueyoshi, Merrill A Ritter, Kenneth E Davis, Randall T Loder

Tatsuya Sueyoshi, Department of Orthopedic Surgery, Kyoto University, Kyoto 606-8507, Japan

Merrill A Ritter, Kenneth E Davis, Center for Hip and Knee Surgery, Mooresville, IN 46158, United States

Randall T Loder, James Whitcomb Riley Children's Hospital, Indianapolis, IN 46202, United States

Author contributions: Sueyoshi T primary contributed to the work and wrote the manuscript; Ritter MA did the surgery and organized the study; Davis KE did the data collection and statistics; Loder RT made some of developmental dysplasia of the hip comments and gave suggestion.

Institutional review board statement: The study was reviewed and approved by the St. Francis Hospital Institutional Review Board.

Informed consent statement: All study participants or their legal guardian provided consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: All the Authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at jrsiresearch1@gmail.com.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Merrill A Ritter, MD, Center for Hip and Knee Surgery, 1199 Hadley Road, Mooresville, IN 46158,

United States. jrsiresearch1@gmail.com
Telephone: +1-317-8345263

Received: January 12, 2016

Peer-review started: January 14, 2016

First decision: March 7, 2016

Revised: August 8, 2016

Accepted: August 17, 2016

Article in press: August 18, 2016

Published online: December 18, 2016

Abstract**AIM**

To determine if there was a seasonal variation in adults undergoing total hip arthroplasty for end stage hip disease due to osteoarthritis (OA) or sequelae of developmental dysplasia of the hip (DDH).

METHODS

The total hip registry from the author's institution for the years 1969 to 2013 was reviewed. The month of birth, age, gender, and ethnicity was recorded. Differences between number of births observed and expected in the winter months (October through February) and non-winter mo (March through September) were analyzed with the χ^2 test. Detailed temporal variation was mathematically assessed using cosinor analysis.

RESULTS

There were 7792 OA patients and 60 DDH patients who underwent total hip arthroplasty. There were more births than expected in the winter months for both the DDH ($P < 0.0001$) and OA ($P = 0.0052$) groups. Cosinor analyses demonstrated a peak date of birth on 1st October.

CONCLUSION

These data demonstrate an increased prevalence of DDH and OA in those patients born in winter.

Key words: Seasonal trend; Winter; Osteoarthritis; Birth month; Developmental hip dysplasia

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The purpose of this study was to determine if there was a seasonal variation undergoing total hip arthroplasty for osteoarthritis (OA) or developmental dysplasia of the hip (DDH). Differences between number of births observed and expected in the winter months and non-winter months were analyzed with the χ^2 test. There were 7792 OA and 60 DDH, and more births than expected in the winter months for both the DDH ($P < 0.0001$) and the OA ($P = 0.0052$) cohorts. These data clearly demonstrated an increased prevalence of DDH and OA in those patients born during the winter months.

Sueyoshi T, Ritter MA, Davis KE, Loder RT. Seasonal variation in adult hip disease secondary to osteoarthritis and developmental dysplasia of the hip. *World J Orthop* 2016; 7(12): 821-825 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/821.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.821>

INTRODUCTION

Total hip arthroplasty (THA) is a standard, successful treatment for end stage hip disease. The etiology of such disease is frequently due to osteoarthritis (OA), osteonecrosis/avascular necrosis (ON/AVN), rheumatoid arthritis (RA) and developmental dysplasia of the hip (DDH). Studies of hip osteoarthritis suggest that childhood deformities or residuals of childhood hip disease often experience accelerated or premature joint degeneration^[1,2]. DDH is a wide spectrum of deformity ranging from mild acetabular dysplasia to complete and fixed dislocation^[3]. Many studies have noted that DDH is more frequent in patients born in the colder months^[4-6]. DDH with residual acetabular dysplasia is often followed by OA of the hip. OA has also been reported to be more frequent in people born in the winter^[7]. The authors wished to determine if there was any seasonal variation in adults who are treated for OA and DDH in the Midwest region of the United States. This will further augment a previous study which noted a seasonal variation in children with DDH in this region^[3].

MATERIALS AND METHODS

A retrospective review of all THAs performed from November 1969 through November 2013 at the author's institution was performed. This review was approved by the local Institutional Review Board. There were 10572 THAs in 8579 patients that met the initial inclusion criteria of primary OA, RA, ON or DDH diagnosis. There were 192 THAs in 157 patients that did not have adequate

Table 1 Month of birth for 7852 patients undergoing total hip arthroplasty for osteoarthritis and sequelae of developmental hip dysplasia

Month of birth	DDH		OA		Temperature (°F)	Precipitation (ins)
	n	%	n	%		
January	10	17	745	9.6	26	2.5
February	6	10	622	8	30.5	2.3
March	3	5	617	7.9	40.7	3.4
April	3	5	585	7.5	51	3.9
May	3	5	582	7.5	61.4	4.5
June	4	7	613	7.9	70.5	4.2
July	3	5	667	8.6	74.3	4.2
August	0	0	675	8.7	72.2	3.9
September	3	5	682	8.8	65.2	3.1
October	14	23	702	9	53.6	3
November	3	5	610	7.8	42.3	3.4
December	8	13	692	8.9	31.2	3.1
Total	60	100	7792	100		41.5

OA: Osteoarthritis; DDH: Developmental hip dysplasia.

demographic data and were excluded from any analysis. The diagnosis was OA in 7792 patients, ON/AVN in 523, RA in 204, and DDH in 60. Those with ON/AVN and RA were then excluded, leaving 9671 THAs in 7852 patients for analysis. Date of birth, age, and gender were gathered from the database of total joint surgeries performed at the authors' institution based on medical records and operation note data at the time of surgery.

The months of the year were divided into winter and non-winter. Winter was defined as October through February, and non-winter as March through September based on local temperatures. The source for the average monthly temperature and precipitation was from the Indiana State Climate Office in Purdue University (<https://climate.agry.purdue.edu/climate/facts.asp>) (Table 1). Differences by winter and non-winter months were evaluated for both the DDH and OA groups. Temporal variation was analyzed using cosinor analysis (see below).

Statistical analysis

Continuous data are reported as the mean \pm standard deviation. Categorical data are reported as frequencies or percentages. Statistical differences between continuous variables were analyzed by the student's *t*-test and between categorical variables by the Pearson's χ^2 test. Statistical Analysis System (SAS) version 9.2 (Cary, NC) was used for *t*-tests and categorical analysis where the expected value was set as the null hypothesis. The Statistical Package for Social Sciences (SPSS) version 12.0 for Windows (SPSS Inc., Chicago, IL, United States) was used for further statistical analysis. The data were subjected to cosinor analysis in an effort to mathematically define any seasonal variation when present. Cosinor analysis^[8,9] determines the best mathematical fit of the data to an equation defined by $F(t) = M + A \cos(\omega t + \phi)$, where M = the mean level (termed mesor), A = the

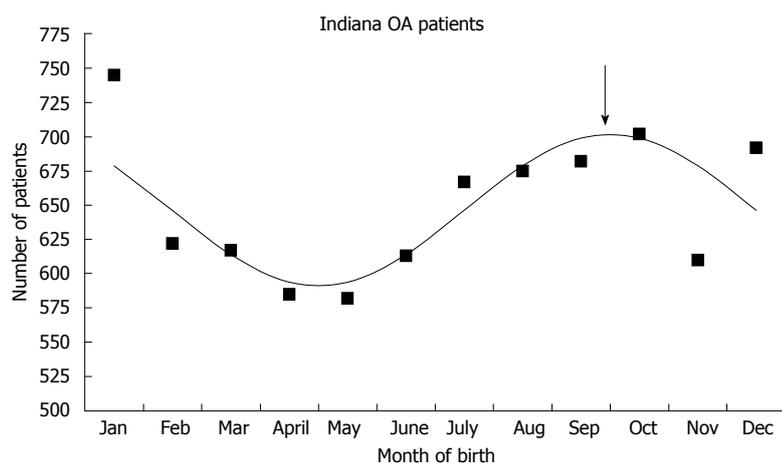


Figure 1 The cosinor fit for Indiana patients with hip osteoarthritis and month of birth. The best fit is represented by the equation: Number of OA births = $646.4 + 55.3 [\cos(36t - 18) - 324]$, where $t = 1$ is January, 2 is February, 3 is March, etc. This was statistically significant ($r^2 = 0.56$, $P = 0.025$). The peak is 1st October (solid arrow). The data points are the black triangles and the best fit represented by the bold black line. OA: Osteoarthritis.

amplitude of the cosine curve, ϕ = acrophase (phase angle of the maximum value), ω = the frequency (which for monthly analysis is $360^\circ/12 = 30^\circ$), and t = time (which in this case is each month). The overall P and r^2 value for the distribution are given for the rhythmic pattern described by the cosinor equation for M , A , and ϕ . The data was analyzed for the entire period of 12 mo as well as decreasing increments of 1 mo. A best monthly fit may not be over a period of 12 mo, but a different time span (*e.g.*, 7 or 6 mo periodicity). Cosinor analyses were performed with ChronoLab 3.0™ software (see Acknowledgement). For all statistical analyses the level of significance was set at $P < 0.05$.

RESULTS

The average age at the time of THA was 55.4 ± 13.6 years in the DDH group and 67.9 ± 11.4 years in the OA group. This age difference was statistically significant ($P < 0.0001$). There were 49 females (81.7%) and 11 males (18.3%) in the DDH and 4160 females (53.4%) and 3632 males (46.6%) in the OA group ($P < 0.0001$). The distribution of birth months for the 7792 OA and 60 DDH patients can be found in Table 1. The number of births in the winter months was much higher than expected in both the DDH [41 of 60 (68.3%) actual, 25 of 60 (41.7%) expected, $P < 0.0001$] and the OA [3371 of 7792 (43.3%) actual, 3247 of 7792 (41.7%) expected, $P < 0.0052$] groups. Cosinor analysis demonstrated an excellent fit for the OA group with a peak on October 1 (Figure 1). There was no good cosinor fit for the DDH group, likely due to the small number.

DISCUSSION

This study demonstrates that both adult DDH and OA patients with end stage hip disease are more frequently born in the colder months. This is similar to pediatric DDH in the previous report^[3] and adult Japanese OA^[7].

Children with DDH undergoing operative treatment demonstrated a peak birth on 15th October^[3], and is essentially the same as the adult OA patients peak on 1st October. Nagamine *et al.*^[7] noted that adult hip osteoarthritis in the Japanese population was more prevalent when the patient was born in the colder months. The authors subjected their data to cosinor analysis and found a peak on 20th January (Figure 2). The Japanese OA peak of 20th January is identical to the 26th January peak in Japanese children with DDH from Kochi, Japan^[3,10].

There are certain limitations to this study. This is a retrospective study and diagnosis of DDH and OA was determined mainly by radiographs and patient history. The diagnosis of OA includes both primary and secondary OA^[11]. Patients undergoing THA are usually at the end stage of hip arthritis making it difficult to distinguish primary from secondary OA. Some patients will have shallow acetabulae, but once the joint space disappears at the lateral aspect of the acetabulum, it is impossible to differentiate between primary and secondary OA. The patient's history may help, but most patients with DDH treated in infancy with a Pavlik harness or other abduction bracing may not be aware of that history; they would not be able to remember it due to their young age at the time of treatment and their parents may not have told them of such treatment. Although the DDH group was small, we still believe that the findings are valid due to the highly significant $P < 0.0001$.

These findings have several possible explanations. First, it is very likely that many of the OA patients had underlying, subtle mild DDH (*e.g.*, minimal acetabular dysplasia). The population of OA, technically the secondary OA, may have just more of DDH than what the authors think. Another possible explanation is that both DDH and OA patients share some common, but as yet unknown, etiology. The possible factors/etiologies that can be invoked are pre-/perinatal maternal factors as well as postnatal environmental factors.

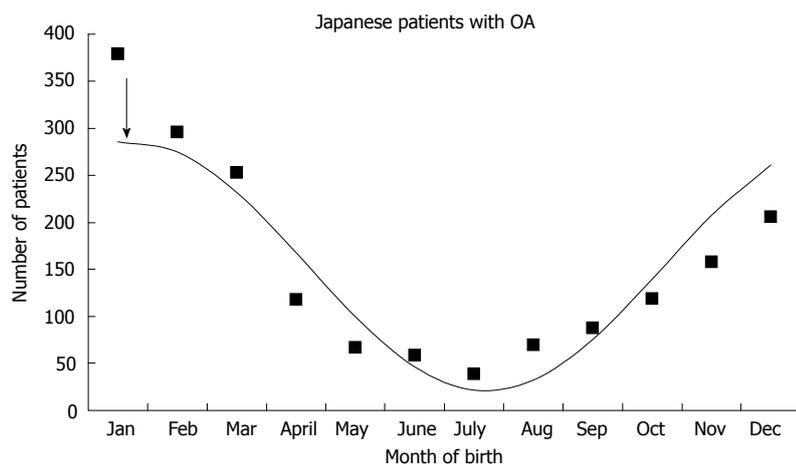


Figure 2 The cosinor fit for Japanese patients with osteoarthritis and month of birth. Data extracted from the study of^[7]. The best fit is represented by the equation: number of OA births = $153.7 + 132.7(\cos 30t - 15) - 21$, where $t = 1$ is January, 2 is February, 3 is March, etc. This was statistically significant ($r^2 = 0.83$, $P < 0.001$). The peak is 20th January (solid arrow). The data points are the black triangles and the best fit represented by the bold black line. OA: Osteoarthritis.

Potential pre-/perinatal factors are a breech birth or difficult delivery^[12]. First born and high-birth-weight babies are at an increased risk of DDH, but those do not exhibit seasonal trend^[6]. Obstetric pelvic insufficiency shows a seasonal variation with a peak in November to December^[13]. In the current study, the authors did not investigate the patients' birth history (pregnancy number or breech/vertex delivery). Since there been no report showing a relationship between osteoarthritis and breech/difficult delivery, it is most likely that residual DDH (minimal acetabular dysplasia) influenced the incidence of OA.

Another potential perinatal factor is relaxin, which stimulates collagenase and alters connective tissue^[14,15]. Collagen metabolism is altered in DDH^[16] with increased joint laxity^[17]. However, the correlation between DDH and relaxin is controversial^[18,19]. In addition, no seasonal variation in relaxin levels has been shown leading to the conclusion that relaxin is not a critical factor. Another possible factor is vitamin D, which is well known to have a seasonal variation with peak levels in the summer^[20,21]. Low maternal levels of vitamin D result in low birth weight infants and increased levels in heavy infants^[22,23]. A report from Norway suggests hip and knee osteoarthritis is more common in those born in the spring months^[24], perhaps due to vitamin D issues.

In conclusion, this study demonstrated that patients undergoing THA for end stage hip disease due to OA or the sequelae of DDH are more commonly born in the colder months. This confirms previous reports noting the same phenomenon in both adult OA and childhood DDH. Further research will be needed to understand this association.

ACKNOWLEDGMENTS

The authors wish to acknowledge the help of Michihiro Kobayashi, MD, PhD, Herman B. Wells Research Center, Department of Pediatrics, Indiana University School of

Medicine who extracted the data from the Japanese study by Haginomori^[10]. ChronoLab 3.0™ software, designed for use on Macintosh™ computers, cannot be purchased. The software used to perform cosinor analyses was provided through the courtesy of Dr. Artemio Mojón and colleagues, Bioengineering and Chronobiology Labs, ETSI Telecomunicación, University of Vigo, Campus Universitario, Vigo (Pontevedra) 36280, Spain. It can be downloaded from their web site at <http://www.tsc.uvigo.es/BIO/Bioing/References.html>. Please kindly acknowledge their generosity when using this software.

COMMENTS

Background

Winter birth has been associated with developmental dysplasia of the hip (DDH) and it was reported recently to be related to hip osteoarthritis (OA). This study aims to investigate the epidemiology of DDH and OA according to the registry of total hip arthroplasty in the authors' institution.

Research frontiers

To the authors' knowledge, this is the first study to present both OA and DDH were associated with winter birth. Reviewing the registry over 40 years, the average age at the surgery was statistically younger in DDH patients than in OA patients. Both DDH and OA patients were more born in winter months than in non-winter months.

Innovations and breakthroughs

Several reports have shown DDH is often caused by swaddling during infancy, which was reported to be one reason DDH is associated with winter birth. The study demonstrated OA also was associated with winter birth. The etiology is still unknown why winter birth influences hip OA, but the study will contribute to elucidate the mechanism of OA and the prevention of hip surgery in the future.

Peer-review

It is an interesting and well-written article.

REFERENCES

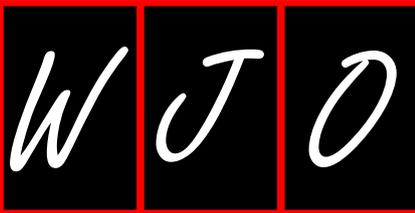
- 1 Harris WH. Etiology of osteoarthritis of the hip. *Clin Orthop Relat Res* 1986; (213): 20-33 [PMID: 3780093]

- 2 **Cooperman DR**, Wallensten R, Stulberg SD. Acetabular dysplasia in the adult. *Clin Orthop Relat Res* 1983; **(175)**: 79-85 [PMID: 6839611 DOI: 10.1097/00003086-198305000-00013]
- 3 **Loder RT**, Shafer C. Seasonal variation in children with developmental dysplasia of the hip. *J Child Orthop* 2014; **8**: 11-22 [PMID: 24500336 DOI: 10.1007/s11832-014-0558-3]
- 4 **Anand JK**, Moden I, Myles JW. Incidence of neonatal hip instability: are there seasonal variations? *Acta Orthop Belg* 1992; **58**: 205-208 [PMID: 1632220]
- 5 **Record RG**, Edwards JH. Environmental influences related to the aetiology of congenital dislocation of the hip. *Br J Prev Soc Med* 1958; **12**: 8-22 [PMID: 13510578 DOI: 10.1136/jech.12.1.8]
- 6 **Robinson GW**. Birth characteristics of children with congenital dislocation of the hip. *Am J Epidemiol* 1968; **87**: 275-284 [PMID: 5647859]
- 7 **Nagamine S**, Sonohata M, Kitajima M, Kawano S, Ogawa K, Mawatari M, Hotokebuchi T. Seasonal trends in the incidence of hip osteoarthritis in Japanese patients. *Open Orthop J* 2011; **5**: 134-137 [PMID: 21584203 DOI: 10.2174/1874325001105010134]
- 8 **Nelson W**, Tong YL, Lee JK, Halberg F. Methods for cosinor-rhythmometry. *Chronobiologia* 1979; **6**: 305-323 [PMID: 548245]
- 9 **Faure A**, Nemoz C, Claustrat B. A graphical and statistical method for investigation of time series in chronobiology according to the cosinor procedure. *Comput Biol Med* 1990; **20**: 319-329 [PMID: 2257732 DOI: 10.1016/0010-4825(90)90011-D]
- 10 **Haginomori K**. A statistical study of congenital dislocation of the hip in the south-western part of Kochi prefecture. *Shikoku Acta Med* 1966; **22**: 112-125
- 11 **Hoaglund FT**, Steinbach LS. Primary osteoarthritis of the hip: etiology and epidemiology. *J Am Acad Orthop Surg* 2011; **9**: 320-327 [PMID: 11575911 DOI: 10.5435/00124635-200109000-00005]
- 12 **Fredensborg N**. Observations in children with congenital dislocation of the hip. *Acta Orthop Scand* 1976; **47**: 175-180 [PMID: 944988 DOI: 10.3109/17453677608989714]
- 13 **Berezin D**. Pelvic insufficiency during pregnancy and after parturition. *Acta Obstet Gynecol Scand Suppl* 1950; **30**: 170-182 [PMID: 14799179 DOI: 10.3109/00016345009164771]
- 14 **Forst J**, Forst C, Forst R, Heller KD. Pathogenetic relevance of the pregnancy hormone relaxin to inborn hip instability. *Arch Orthop Trauma Surg* 1997; **116**: 209-212 [PMID: 9128773 DOI: 10.1007/BF00393711]
- 15 **Saugstad LF**. Persistent pelvic pain and pelvic joint instability. *Eur J Obstet Gynecol Reprod Biol* 1991; **41**: 197-201 [PMID: 1936503 DOI: 10.1016/0028-2243(91)90024-F]
- 16 **Jensen BA**, Reimann I, Fredensborg N. Collagen type III predominance in newborns with congenital dislocation of the hip. *Acta Orthop Scand* 1986; **57**: 362-365 [PMID: 3788503 DOI: 10.3109/17453678608994412]
- 17 **Carr AJ**, Jefferson RJ, Benson MK. Joint laxity and hip rotation in normal children and in those with congenital dislocation of the hip. *J Bone Joint Surg Br* 1993; **75**: 76-78 [PMID: 8421041 DOI: 10.1097/01241398-199307000-00043]
- 18 **Hinderaker T**, Daltveit AK, Irgens LM, Udén A, Reikerås O. The impact of intra-uterine factors on neonatal hip instability. An analysis of 1,059,479 children in Norway. *Acta Orthop Scand* 1994; **65**: 239-242 [PMID: 8042471 DOI: 10.3109/17453679408995446]
- 19 **Vogel I**, Andersson JE, Uldbjerg N. Serum relaxin in the newborn is not a marker of neonatal hip instability. *J Pediatr Orthop* 1998; **18**: 535-537 [PMID: 9661868]
- 20 **Stryd RP**, Gilbertson TJ, Brunden MN. A seasonal variation study of 25-hydroxyvitamin D3 serum levels in normal humans. *J Clin Endocrinol Metab* 1979; **48**: 771-775 [PMID: 429522 DOI: 10.1210/jcem-48-5-771]
- 21 **Andersen R**, Mølgaard C, Skovgaard LT, Brot C, Cashman KD, Chabros E, Charzewska J, Flynn A, Jakobsen J, Kärkkäinen M, Kiely M, Lamberg-Allardt C, Moreiras O, Natri AM, O'brien M, Rogalska-Niedzwiedz M, Ovesen L. Teenage girls and elderly women living in northern Europe have low winter vitamin D status. *Eur J Clin Nutr* 2005; **59**: 533-541 [PMID: 15714215 DOI: 10.1038/sj.ejcn.1602108]
- 22 **Aghajafari F**, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: systematic review and meta-analysis of observational studies. *BMJ* 2013; **346**: f1169 [PMID: 23533188 DOI: 10.1136/bmj.f1169]
- 23 **Christesen HT**, Elvander C, Lamont RF, Jørgensen JS. The impact of vitamin D in pregnancy on extraskeletal health in children: a systematic review. *Acta Obstet Gynecol Scand* 2012; **91**: 1368-1380 [PMID: 23210535 DOI: 10.1111/aogs.12006]
- 24 **Fønnebo V**. Arthrosis of the hip and knee: environmental causes in the first year of life? A study of 1405 cases of arthrosis in north Norway 1984-1989. *Arctic Med Res* 1995; **54**: 151-154 [PMID: 7669129]

P- Reviewer: Lee SH, Sebestyén A **S- Editor:** Kong JX

L- Editor: A **E- Editor:** Lu YJ





Observational Study

Effect of introducing an online system on the follow-up of elbow arthroplasty

Jetske Viveen, Ante Prkic, Bertram The, Koen LM Koenraadt, Denise Eygendaal

Jetske Viveen, Ante Prkic, Bertram The, Denise Eygendaal, Upper Limb Unit, Department of Orthopaedic Surgery, Amphia Hospital, 4818 CK Breda, The Netherlands

Koen LM Koenraadt, Foundation for Orthopedic Research, Care & Education, Amphia Hospital, 4818 CK Breda, The Netherlands

Denise Eygendaal, Department of Orthopaedic Surgery, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam-Zuidoost, The Netherlands

Author contributions: Viveen J data collection and drafting the article; Prkic A drafting the article; The B critical revision of the article; Koenraadt KLM data analysis and interpretation and critical revision of the article; Eygendaal D critical revision of the article and final approval of the version to be published.

Institutional review board statement: The medical ethical committee waived ethical approval for the study as no new intervention or treatment was initiated.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Jetske Viveen, MSc, Upper Limb Unit, Department of Orthopaedic Surgery, Amphia Hospital, Molengracht 21, 4818 CK Breda, The Netherlands. jetskeviveen@gmail.com
Telephone: +31-076-5955578
Fax: +31-076-5953819

Received: June 23, 2016
Peer-review started: June 27, 2016
First decision: August 11, 2016
Revised: August 22, 2016
Accepted: October 25, 2016
Article in press: October 27, 2016
Published online: December 18, 2016

Abstract

AIM

To evaluate the effect of introducing a structured online follow-up system on the response rate.

METHODS

Since June 2015 we have set up an electronic follow-up system for prosthesis in orthopedic patients. This system allows prospective data gathering using both online and paper questionnaires. In the past all patients received questionnaires on paper. This study includes only patients who received elbow arthroplasty. Response rates before and after introduction of the online database were compared. After the implementation, completeness of the questionnaires was compared between paper and digital versions. For both comparisons Fisher's Exact tests were used.

RESULTS

A total of 233 patients were included in the study. With the introduction of this online follow-up system, the overall response rate increased from 49.8% to 91.6% ($P < 0.01$). The response rate of 92.0% in the paper group was comparable to 90.7% in the online group ($P > 0.05$).

Paper questionnaires had a completeness of 54.4%, which was lower compared to the online questionnaires where we reached full completeness ($P < 0.01$). Furthermore, non-responders proved to be younger with a mean age of 52 years compared to a mean age 62 years of responders ($P < 0.05$).

CONCLUSION

The use of a structured online follow-up system increased the response rate. Moreover, online questionnaires are more complete than paper questionnaires.

Key words: Patient reported outcome measures; Elbow; Follow-up; Arthroplasty; Online; Database

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Since the last decade, increasing attention is paid on patient reported outcome measures (PROMs) and several online follow-up systems became available to collect PROMs. The purpose of this article was to evaluate the introduction of a structured online follow-up system in order to facilitate analysis of data.

Viveen J, Prkic A, The B, Koenraadt KLM, Eygendaal D. Effect of introducing an online system on the follow-up of elbow arthroplasty. *World J Orthop* 2016; 7(12): 826-831 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/826.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.826>

INTRODUCTION

In 2002, the Swedish Hip Arthroplasty Registry started using patient reported outcome measures (PROMs) on a national scale. In 2011, patients' response rates of up to 90.2% were reported for this registry, Several other national registries have followed their model. In general, most PROMs data are collected from total hip replacement patients. None of the registries included mandatory PROMs on elbow arthroplasty in their dataset.

Nevertheless, PROMs are increasingly used to evaluate the outcome of surgical procedures in patient care and in clinical orthopaedic research projects^[1-4]. These subjective outcomes may be even of more clinical importance than objective outcomes such as range of motion, since patient satisfaction is determined in a complex multifactorial way and does not always correlate well with easy-to-measure objective endpoints.

Unfortunately, in all medical fields researchers and clinicians have to deal with non-responders. This can potentially lead to biased results. And although statistical methods can be employed in an attempt to reduce this effect, it is better to achieve a high response rate to begin with. Therefore encouragement of patients to complete questionnaires is necessary, ideally by using simple and attractive tools.

Especially in patients who received elbow prostheses a structured follow-up is important, as the survival rate of elbow prosthesis is not as high as the rate of hip- and knee arthroplasties^[3]. Despite of several technical improvements of the implants, complications still plague patients with a total elbow arthroplasty. Symptoms of a loosened elbow prosthesis are sometimes unclear and unspecific. This makes recognition at an early stage difficult. Nevertheless, it is essential to have the earliest detection as possible, since loosening of the prosthesis may cause irreversible bone destruction^[5-8].

Since the last decade, several online follow-up systems became available to collect PROMs. Before these systems became available, all questionnaires were sent manual on paper. In the current study we want to report on the advantages and disadvantages of using an online follow-up system. The aim of this study is to evaluate the effect of introducing a structured online follow-up system, as our hypothesis was to increase the response rate in order to obtain a complete follow-up of patients who received elbow arthroplasty.

MATERIALS AND METHODS

This study includes patients who have received surgery at our hospital for four types of elbow arthroplasties; total elbow prosthesis, radial head prosthesis, radiocapitellar prosthesis and revisions of aforementioned prosthesis. Patients were excluded if they were cognitive or physical impaired and therefore unable to complete questionnaires or to visit the outpatient clinic. In total 233 patients met the inclusion criteria and were included for the study.

Demographic data are presented in Table 1. Ninety-nine patients received a total elbow arthroplasty, 14 patients a radiocapitellar prosthesis, 68 patients a radial head prosthesis and 52 patients received revision surgery of aforementioned prosthesis. There were 60 men and 173 woman included. Mean age at surgery was 61 years (SD 13). For further details for each type of elbow arthroplasty see Table 1.

Since June 2015 we have set up an electronic follow-up system (online PROMs, Interactive Studios, Rosmalen, The Netherlands), which allows prospective data gathering using online questionnaires. Online questionnaires are sent automatically at multiple follow-up moments after surgery or manual if patients prefer paper questionnaires. All questionnaires we use are valid in our language. Additional physical examination results can be added manually during reassessment at the outpatient clinic.

Until this introduction all patients received questionnaires on paper. Questionnaires were sent regarding the same follow-up moments, but monitoring was poor since no structured (online) system was available. Patients who received surgery before implementation of the online system are added to the system as well. Questionnaires sent after June 2015 for this group of patients counted as post implementation questionnaires.

When elbow arthroplasty surgery is planned at the

Table 1 Demographic data of all patients divided per type of prosthesis

	Total elbow prosthesis	Radiocapitellar prosthesis	Radial head prosthesis	Revision surgery	Total
Patients (<i>n</i>)	99	14	68	52	233
Sex					
Man	22	7	19	12	60
Woman	77	7	49	40	173
Age (yr)					
Mean (SD)	69 (4)	56 (7)	50 (13)	61 (13)	61 (13)

outpatient clinic and the patient gives written informed consent for use of the data for research, the patient is added to our database. The email addresses are added to the online-system. The database sends a preoperative questionnaire automatically close before surgery. In case of missing email addresses, patients who visit the outpatient clinic for reassessment are asked for their email address, so they can receive the questionnaires regarding the next follow-up moments by email. When the patient prefers paper questionnaires, results are manually added to the electronic system.

This online planning system makes it possible to remind patients and nurse practitioners (NP) to send paper questionnaires and to schedule an appointment as well. Thereby a notification on the dashboard of the online-system shows up if we did not receive response to the questionnaire within two weeks. At our institution we use a protocol for non-responders both in the email and paper group. A second questionnaire is sent after two weeks and if we still do not receive response after four weeks since the first effort, the NP calls the patient to remind them. If patients do not want to participate anymore they can be deactivated in the system.

We intend to achieve a full preoperative PROMs data capture rate. Because we collect PROMs in the trauma department too, we are used to complete the questionnaires retrospectively with maximum scores in baseline in case of acute trauma. The pre-operative questionnaires serve as a baseline measurement. The post-operative follow-up protocol consists of a visit to the outpatient clinic after one, three, five, seven and ten years including questionnaires. On every occasion, the surgeon or the NP sees the patient and a plain X-ray is made.

Since the introduction the pre- and postoperative patients' part of the questionnaires are slightly different. The preoperative questionnaire consists of the Euroqol five dimensions (EQ-5D), the Oxford Elbow Score (OES) and the Visual Analogue pain Scales (VAS 0-10) in rest and activity. Thereby the patient is asked if they did have surgery on their elbow before. If the answer is yes, we want to know when the surgery took place and what kind of surgery it was.

The postoperative questionnaires consist of the EQ-5D, the OES and the VAS 0-10 in rest and activity too. In addition, the patient is asked how satisfied they are with the result of the surgery and whether they would recommend the received therapy for their elbow to

colleagues, friends or family members. These questions are answered on a seven-point scale (satisfaction) and ten-point scale (recommendation). Before the introduction the pre- and postoperative questionnaires were the same and consisted of the OES and VAS pain in rest and activity.

Statistical analysis

For every follow-up moment in each group we determined the number of questionnaires sent and the number of questionnaires we received. We have added these numbers for every group. We compared response rates before and after the introduction of the online database in June 2015. After implementation of the online system we compared the online- and the paper questionnaires group on response rate, completeness and mean age. In addition, we compared the mean age of responders and non-responders in both groups after implementation. Differences on outcome parameters before and after the introduction of the online database were compared using T-tests for normally distributed data and Fisher's Exact test for dichotomous data.

RESULTS

Before vs after the introduction of the online database

Before June 2015 we achieved an overall response rate of 49.8% on 616 sent questionnaires. After implementation of the online database 143 questionnaires were sent and the response rate increased to 91.6% ($P < 0.01$) (Figure 1). Using the online system we captured full response rates both in patients who received radiocapitellar prosthesis and patients who received revision surgery. In patients who received a total elbow arthroplasty and those who received a radial head prosthesis response rates of respectively 90.0% and 83.3% were revealed (Table 2).

Paper vs online after the introduction of the online database

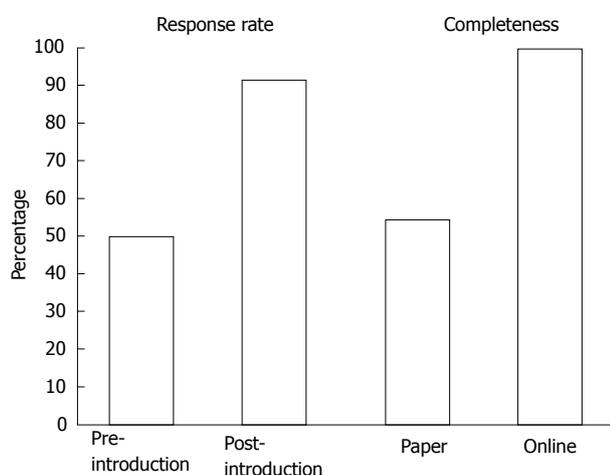
Since the implementation 100 questionnaires were sent on paper and 43 online. We received 92 paper questionnaires and 39 online questionnaires. With a completeness of 54.4% of paper questionnaires, completeness was lower compared to the online questionnaires where we reached full completeness ($P < 0.01$) (Figure 1). The mean age of 63 years (SD 12) of patients who completed the questionnaires on paper was comparable to the mean age

Table 2 Results before vs after introduction of the online database

	Total elbow prosthesis	Radiocapitellar prosthesis	Radial head prosthesis	Revision surgery	Total
Questionnaires sent in total					
Before introduction	212	24	245	135	616
After introduction	69	8	36	30	143
Response rate (%)					
Before introduction	57.90%	45.80%	40.40%	54.10%	49.80%
After introduction	89.90%	100%	83.30%	100%	91.60%
Email address known (<i>n</i>)	43	5	26	21	95

Table 3 Paper vs online after the introduction of the online database

	Total elbow prosthesis	Radio-capitellar prosthesis	Radial head prosthesis	Revision surgery	Total
Questionnaires sent in total					
Paper	49	5	24	22	100
Online	20	3	12	8	43
Response rate					
Paper	91.90%	100.00%	83.30%	100.00%	92.00%
Online	90.00%	100.00%	83.30%	100.00%	90.70%
Completeness of questionnaires					
Paper	48.90%	40.00%	65.00%	59.10%	54.40%
Online	100.00%	100.00%	100.00%	100.00%	100.00%
Mean age (yr)					
Paper (SD)	68 (8)	58 (8)	50 (14)	63 (10)	63 (12)
Online (SD)	68 (8)	50 (3)	50 (13)	55 (16)	59 (14)
Mean age (yr)					
Responders (SD)	68 (8)	55 (7)	50 (13)	61 (13)	62 (13)
Non-responders (SD)	67 (10)	-	36 (13)	-	52 (19)

**Figure 1** Response rate and completeness.

of 59 years (SD 14) of patients in the online group. If we combine non-responders in the paper and online group, non-responders proved to be younger with a mean age of 52 years (SD 19) compared to a mean age of 62 years (SD 13) of responders ($P < 0.05$). For further details see Table 3.

Online questionnaires

Since the introduction we have collected 95 (41%) email addresses of all elbow arthroplasty patients. The mean age of patients using an email address was 59

years (SD 14). The mean completion time of online questionnaires was 5.2 min (SD 3). Completion times of paper questionnaires were not available.

DISCUSSION

The results of the current study are promising with an increase in response rate from 49.8% to 91.6%. After implementation good response rates are reported both for paper and online questionnaires. In addition online questionnaires were more complete compared to paper questionnaires and non-responders proved to be younger compared to responders.

Several factors might have increased the response rate after the introduction of the online system. As the dashboard function reminds the NP to send paper questionnaires and to be aware of non-response of sent questionnaires, structure is provided regarding follow-up moments. Furthermore, the effort that was previously put into collecting and storing paper versions, is now put into attempts to collect the data in non-responders, since this information is easily fed back by the system. In addition, the amount of paper questionnaires decreased since the online system sends online questionnaires automatically. Therefore, less printing of questionnaires, enveloping, filing, and manual transfer of data from the paper questionnaire to the database is needed anymore. Hence, all these factors together resulted in a huge increase of response rate up to 91.6%.

We also observed some interesting findings on questionnaires sent after the introduction of the online system. At first, we obtained full completeness of online questionnaires compared to 54.4% completeness of paper questionnaires. This is another benefit of using an online system. Online it is impossible to skip questions, while in paper questionnaires researchers and clinicians have to deal with incomplete questionnaires, which accounts for data loss. Secondly, in the current study non-responders proved to be younger compared to the mean age of responders. This is comparable to the results of two other studies^[5,6]. On the contrary, other studies associated non-response with older age^[2,9-11]. The reason of higher non-response rates in younger patients is unclear, but it could be a result of busy lifestyle and low priority in completing questionnaires. With a mean completion time of 5.2 min we think it is reachable to encourage patients to complete our questionnaires. Moreover, in literature the completion times of paper questionnaires are reported to be significant longer compared to online questionnaires when data entry time is studied^[7].

The last noticeable results of the study was the relatively high mean age of patients in the current study was, which probably leads to fewer email addresses, because this generation is not used to computers and/or email^[9]. Nevertheless, the decision to use this group of patients was conscious since a structured follow-up for patients who received an elbow arthroplasty is important as asymptomatic aseptic loosening may cause irreversible loss of bone stock. Hence, in addition to the increase in response rate by using an online system, the current study revealed: A higher completeness using digital-compared to paper questionnaires, that non-response rate was higher in younger subjects and that online questionnaires only took 5.2 min to complete.

While the response rate increased greatly in questionnaires, no show on follow-up moments at the outpatient clinic is still a problem. Arguments we frequently encounter are high costs of the deductible, not having any complaints of the elbow and dependency of elderly people on relatives for driving. Unfortunately, at the moment there is no scientific evidence on the number of reassessments we need to perform to be sufficient in follow-up. However, if patients do not want to be reassessed at the outpatient clinic, questionnaires can be sent anyway. For future research, with a prolonged follow-up, patterns in PROMs outcomes of elbow arthroplasties may be distinguished, so deterrence may be detected earlier and attacked more effectively by, for example, revision surgery. Therefore, with more data, we hope to be able to predict the clinical course per patient and to provide still better patient care.

The current study has two limitations. At first the time since the introduction of the online system in June 2015 is short. Although time is short, we can already report promising results. Thereby in the future we predict more patients to have an email address. We

are convinced this transition from a less online oriented population to a more online oriented population will ensure even better results using an online follow-up system. Further studies are required to evaluate the results on long-term. In addition, the response rate after the implementation of the system could be biased by the effort that was put into collecting questionnaires. Although, this effort could have been put into collecting, since structure was given to follow-up by the dashboard function of the system.

In conclusion, the results of the current study are promising. A structured online system could increase both the response rate and completeness of questionnaires. Further studies are required to report on the mid- and long-term results of the introduction of a structured online follow-up system.

ACKNOWLEDGMENTS

We would like to thank our nurse practitioner, Yvonne de Deugd, for the effort she has put into collecting questionnaires and email addresses.

COMMENTS

Background

Since the last decade, several online follow-up systems became available to collect patient reported outcome measures (PROMs). Before these systems became available, all questionnaires were sent manual on paper. In the current study the authors want to report on the advantages and disadvantages of using an online follow-up system.

Research frontiers

In 2002, the Swedish Hip Arthroplasty Registry started using PROMs on a national scale. Since good response rates were reported in 2011, several other national registries have followed their model. However no literature is available on the effect of introducing an online database. This is the first study reporting on the increased response rate using an online follow-up system.

Innovations and breakthroughs

In the recent years several online databases became available to collect PROMs. The present study represents the effect of introducing an online database on the follow-up of patients who received elbow arthroplasty. The major findings of the study were both an increased response rate and completeness of questionnaires using an online database.

Applications

The data in this study suggested that an online follow-up system could both increase the response rate and completeness of questionnaires. According to the findings of the current study, they can recommend the use of an online database in order to improve the follow-up of patients who have received (elbow) arthroplasty.

Terminology

PROMs are patient reported outcome measures, which are frequently used for follow-up of patients who have received surgery.

Peer-review

It is a well presented, interesting early stage pilot study. Available papers concerning the use of online follow-up databases are rare or non-existing. However, it is about a relevant topic in orthopaedic surgery.

REFERENCES

- 1 **Calvert M**, Blazeby J, Altman DG, Revicki DA, Moher D, Brundage MD. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. *JAMA* 2013; **309**: 814-822 [PMID: 23443445 DOI: 10.1001/jama.2013.879]
- 2 **Emberton M**, Black N. Impact of non-response and of late-response by patients in a multi-centre surgical outcome audit. *Int J Qual Health Care* 1995; **7**: 47-55 [PMID: 7640918]
- 3 **Fevang BT**, Lie SA, Havelin LI, Skredderstuen A, Furnes O. Results after 562 total elbow replacements: a report from the Norwegian Arthroplasty Register. *J Shoulder Elbow Surg* 2009; **18**: 449-456 [PMID: 19393935 DOI: 10.1016/j.jse.2009.02.020]
- 4 **Franklin PD**, Harrold L, Ayers DC. Incorporating patient-reported outcomes in total joint arthroplasty registries: challenges and opportunities. *Clin Orthop Relat Res* 2013; **471**: 3482-3488 [PMID: 23897504 DOI: 10.1007/s11999-013-3193-2]
- 5 **Hutchings A**, Neuburger J, Grosse Frie K, Black N, van der Meulen J. Factors associated with non-response in routine use of patient reported outcome measures after elective surgery in England. *Health Qual Life Outcomes* 2012; **10**: 34 [PMID: 22462512 DOI: 10.1186/1477-7525-10-34]
- 6 **Imam MA**, Barke S, Stafford GH, Parkin D, Field RE. Loss to follow-up after total hip replacement: a source of bias in patient reported outcome measures and registry datasets? *Hip Int* 2014; **24**: 465-472 [PMID: 24970318 DOI: 10.5301/hipint.5000141]
- 7 **Kesterke N**, Egeter J, Erhardt JB, Jost B, Giesinger K. Patient-reported outcome assessment after total joint replacement: comparison of questionnaire completion times on paper and tablet computer. *Arch Orthop Trauma Surg* 2015; **135**: 935-941 [PMID: 25957980 DOI: 10.1007/s00402-015-2222-x]
- 8 **Krenek L**, Farnig E, Zingmond D, SooHoo NF. Complication and revision rates following total elbow arthroplasty. *J Hand Surg Am* 2011; **36**: 68-73 [PMID: 21193128 DOI: 10.1016/j.jhssa.2010.09.036]
- 9 **Newhouse N**, Lupiáñez-Villanueva F, Codagnone C, Atherton H. Patient use of email for health care communication purposes across 14 European countries: an analysis of users according to demographic and health-related factors. *J Med Internet Res* 2015; **17**: e58 [PMID: 25798912 DOI: 10.2196/jmir.3700]
- 10 **Rolfson O**, Kärrholm J, Dahlberg LE, Garellick G. Patient-reported outcomes in the Swedish Hip Arthroplasty Register: results of a nationwide prospective observational study. *J Bone Joint Surg Br* 2011; **93**: 867-875 [PMID: 21705555 DOI: 10.1302/0301-620X.93B7.25737]
- 11 **Sales AE**, Plomondon ME, Magid DJ, Spertus JA, Rumsfeld JS. Assessing response bias from missing quality of life data: the Heckman method. *Health Qual Life Outcomes* 2004; **2**: 49 [PMID: 15373945]

P- Reviewer: Drosos GI, Malik H, van den Bekerom MPJ

S- Editor: Qiu S **L- Editor:** A **E- Editor:** Lu YJ



Observational Study

Surgical appgar score predicts early complication in transfemoral amputees: Retrospective study of 170 major amputations

Christian Wied, Nicolai B Foss, Morten T Kristensen, Gitte Holm, Thomas Kallemoose, Anders Troelsen

Christian Wied, Morten T Kristensen, Gitte Holm, Thomas Kallemoose, Anders Troelsen, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, DK-2650, Denmark

Nicolai B Foss, Department of Anesthesiology and Intensive Care, Copenhagen University Hospital Hvidovre, DK-2650, Denmark

Morten T Kristensen, Physical Medicine and Rehabilitation Research-Copenhagen, Department of Physical Therapy, Copenhagen University Hospital Hvidovre, DK-2650, Denmark

Thomas Kallemoose, Clinical Research Centre, Copenhagen University Hospital Hvidovre, DK-2650, Denmark

Author contributions: All the authors contributed to the manuscript.

Institutional review board statement: This retrospective study was undertaken using data from medical records only. The local ethics committee approved the protocol. Protocol: H-6-2014-FSP-026.

Informed consent statement: Our retrospective study contained data from medical records only. The study was registered at the regional data protection agency (04.12.2012) (j. no. 01975 HVH-2012-053).

Conflict-of-interest statement: The authors declare that they have no conflicts of interest. No benefits in any form have been received or will be received from any commercial party related directly or indirectly to the subject of this article.

Data sharing statement: The data from this study will be available on request.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on

different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Christian Wied, MD, Department of Orthopedic Surgery, Copenhagen University Hospital Hvidovre, Kettegaard Alle 30, DK-2650, Denmark. chr.wied@gmail.com
 Telephone: +45-20616831
 Fax: +45-38623782

Received: June 22, 2016

Peer-review started: June 27, 2016

First decision: August 11, 2016

Revised: September 19, 2016

Accepted: October 25, 2016

Article in press: October 27, 2016

Published online: December 18, 2016

Abstract

AIM

To assess whether the surgical appgar score (SAS) is a prognostic tool capable of identifying patients at risk of major complications following lower extremity amputations surgery.

METHODS

This was a single-center, retrospective observational cohort study conducted between January 2013 and April 2015. All patients who had either a primary transtibial amputation (TTA) or transfemoral amputation (TFA) conducted at our institution during the study period were assessed for inclusion. All TTA patients underwent a standardized one-stage operative procedure (ad modum Persson amputation) performed approximately 10 cm below the knee joint. All TTA procedures were performed

with sagittal flaps. TFA procedures were performed in one stage with amputation approximately 10 cm above the knee joint, performed with anterior/posterior flaps. Trained residents or senior consultants performed the surgical procedures. The SAS is based on intraoperative heart rate, blood pressure and blood loss. Intraoperative parameters of interest were collected by revising electronic health records. The first author of this study calculated the SAS. Data regarding major complications were not revealed to the author until after the calculation of SAS. The SAS results were arranged into four groups (SAS 0-4, SAS 5-6, SAS 7-8 and SAS 9-10). The cohort was then divided into two groups representing low-risk ($SAS \geq 7$) and high-risk patients ($SAS < 7$) using a previously established threshold. The outcome of interest was the occurrence of major complications and death within 30-d of surgery.

RESULTS

A logistic regression model with SAS 9-10 as a reference showed a significant linear association between lower SAS and more postoperative complications [all patients: OR = 2.00 (1.33-3.03), $P = 0.001$]. This effect was pronounced for TFA [OR = 2.61 (1.52-4.47), $P < 0.001$]. A significant increase was observed for the high-risk group compared to the low-risk group for all patients [OR = 2.80 (1.40-5.61), $P = 0.004$] and for the TFA sub-group [OR = 3.82 (1.5-9.42), $P = 0.004$]. The AUC from the models were estimated as follows: All patients = [0.648 (0.562-0.733), $P = 0.001$], for TFA patients = [0.710 (0.606-0.813), $P < 0.001$] and for TTA patients = [0.472 (0.383-0.672), $P = 0.528$]. This indicates moderate discriminatory power of the SAS in predicting postoperative complications among TFA patients.

CONCLUSION

SAS provides information regarding the potential development of complications following TFA. The SAS is especially useful when patients are divided into high- and low-risk groups.

Key words: Surgical apgar score; Mortality; Transfemoral amputation; Post-operative complication; Lower extremity amputation

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This study presents new knowledge regarding the use of Surgical Apgar Score (SAS) in dysvascular lower extremity amputations (LEA) surgery. There is a significant increase in complications with a low SAS after LEA surgery. This is even more pronounced when the transfemoral amputation (TFA) sub-group is analyzed separately. Thus, for a TFA patient with a $SAS < 7$, the odds of a major complication or death is four times greater than for a patient with a $SAS \geq 7$. ROC analysis confirms the discriminatory power of the SAS approach among the TFA patients. However, the SAS model proved to be of no prognostic value in the transtibial amputation group.

Wied C, Foss NB, Kristensen MT, Holm G, Kallemsø T, Troelsen A. Surgical apgar score predicts early complication in transfemoral amputees: Retrospective study of 170 major amputations. *World J Orthop* 2016; 7(12): 832-838 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/832.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.832>

INTRODUCTION

The surgical apgar score (SAS) has a strong correlation with the occurrence of major complications or death within 30-d following general and vascular surgery^[1-4]. The scoring system is based on three intraoperative variables: Lowest mean arterial pressure, lowest heart rate and estimated intraoperative blood loss. The score seems to be irrelevant to several orthopedic sub-specialties^[5,6]. However, there is a lack of knowledge regarding the utility of the score in the field of lower extremity amputations (LEA). An increasing number of high-risk patients are undergoing amputations^[7]. They diverge from standard orthopedic patients due to their high age and many comorbidities^[8]. Studies show that their associated 30-d postoperative mortality is up to 30%^[9], a rate unmatched in the orthopedic specialty. Our aim with this study is to assess whether the SAS is a prognostic tool capable of identifying patients at risk of major complications following LEA surgery.

MATERIALS AND METHODS

This was a single-center, retrospective observational cohort study conducted between January 2013 and April 2015. All patients who had either a primary transtibial amputation (TTA) or transfemoral amputation (TFA) at our institution during the study period were assessed for inclusion. Exclusion criteria included: Re-amputations, a combination of amputation and removal of intramedullary nails and patients with incomplete data registrations. Patients were identified through our local operation database. All patients eligible for inclusion were included. The decision regarding the amputation level was made by senior consultants taking into account skin perfusion pressure measurement results and patient general condition. All TTA patients underwent a standardized one-stage operative procedure (admodum Persson amputation)^[10] performed approximately 10 cm below the knee joint. All TTA procedures were performed with sagittal flaps. The TFA procedures were performed in one stage approximately 10 cm above the knee joint, performed with anterior/posterior flaps. Trained residents or senior consultants performed the surgical procedures. The tourniquet, when used, was inflated around the femur to a pressure of 100 mmHg above systolic blood pressure^[11]. Standardized care was provided for all patients including standards for fluid replacement and thromboprophylaxis. Initial postoperative rehabilitation programs were initiated

Table 1 Calculation of surgical apgar score

	0 point	1 point	2 points	3 points	4 points
Estimated blood loss, mL	> 1000	601 - 1000	101-600	< 100	-
Lowest mean arterial pressure, mmHg	< 40	40-54	55-69	> 70	-
Lowest heart rate, beats per min	> 85	76-85	66-75	56-65	< 55

on the first postoperative day if patients could cooperate.

Intraoperative parameters of interest were collected by reviewing electronic health records. The first author of this study calculated the SAS by following the algorithm described in Table 1. Data regarding major complications were not revealed to the author until after the calculation of SAS. SAS results were arranged into four groups (SAS 0-4, SAS 5-6, SAS 7-8 and SAS 9-10) as proposed by Gawande *et al.*^[2]. The cohort was then divided into two groups representing low-risk (SAS \geq 7) and high-risk (SAS < 7) patients using a previously established threshold^[5,6,12]. The outcome of interest was the occurrence of major complications and death within 30-d of surgery. The definitions of major complications were in accordance with Gawande *et al.*^[2] from their original study of the field^[2]. This included the following: Bleeding requiring \geq 4 units of red cell transfusion within 3 d following the operation, acute renal failure (postoperative creatinine > 200 μ mol/L), acute myocardial infarction, X-ray verified pneumonia, pulmonary embolism, stroke, sepsis and death. The data collectors within this group were cautious not to register preexisting diseases as postoperative complications. The findings were double-checked by two independent researchers to avoid over-registration of complications. The outcomes were omitted compared to Gawande's original work due either to their rare occurrence in amputation surgery or lack of registration in the electronic charts. The study was approved by the local ethics committee and registered at the regional data protection agency (04.12.2012) (j. no. 01975 HVH-2012-053).

Continuous data are presented as median values with interquartile ranges (IQR) or mean values with standard deviations (SD). Comparison between TTA and TFA patients was performed using the t-test or the Wilcoxon rank sum test. Categorical data are presented as numbers with percentages. Comparison between TTA and TFA patients was performed using the chi-squared test or Fisher's exact test. Logistic regression models analyzed the relationship between complications and SAS. Odds ratios (OR) were estimated both for each group level with SAS 9-10 as a reference level and as an average change between levels in the SAS groups to estimate a linear effect across the groups. Both models were analyzed for all patients as one group and were stratified for TFA and TTA procedures.

The discriminatory accuracy of the SAS was evaluated by ROC analysis. The results were expressed

as area under the curve (AUC) and related 95%CI. Logistic regression for complications was made based on the high- and low-risk grouping to evaluate the level of increased risk based on the threshold. This was performed both for all patients as one group and on a stratified basis for the TFA and the TTA procedures. The fits of the logistic regression models were evaluated using the Hosmer-Lemeshow goodness-of-fit test. A p-value of 0.05 was considered statistically significant. All analyses were performed by a biostatistician working with R 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

One hundred seventy out of 228 consecutive patients who underwent LEA surgery during the two-year study period were included in the final analysis. In total, 58 patients were excluded due to re-amputation ($n = 37$) or missing data ($n = 21$). The preoperative characteristics are shown in Table 2 and the intraoperative characteristics in Table 3. The overall incidence of major complications and deaths is shown in Table 4 and in relation to the SAS groups in Table 5, which also includes the results from the regression model comparing the individual groups to the reference group. There was a significant linear association demonstrated between SAS group level [OR = 2.00 (1.33-3.03), $P = 0.001$] and complications or death, Table 5. This effect was statistically significant for the TFA group [OR = 2.61 (1.52-4.47), $P < 0.001$] but not for the TTA sub-group [OR = 1.12 (CI: 0.55-2.29), $P = 0.76$]. A significant increase in complications or deaths was observed in the high-risk group (SAS < 7) compared to the low-risk group (SAS \geq 7) [OR = 2.80 (1.40-5.61), $P = 0.004$]. Corresponding results when the TFA and TTA groups were analyzed separately were [TFA: OR = 3.81 (1.5-9.42), $P = 0.004$], [TTA: OR = 1.69 (0.56-5.12), $P = 0.35$]. The results of the Hosmer-Lemeshow Goodness-of-fit test for the four models all had P -values close to 1, supporting the model assumptions. The results of ROC analysis are shown in Figure 1. The cut-off point of SAS \geq 7 was found to be optimal when compared to all other cut-off points based on the specificity and sensitivity as evaluated by the Youden index. The AUC from the models were estimated as follows: All patients = 0.648 (0.562-0.733, $P = 0.001$), TFA = 0.710 (0.606-0.813, $P < 0.001$) and TTA = 0.472 (0.383-0.672, $P = 0.528$).

DISCUSSION

This study presents new knowledge regarding the use of the SAS in dysvascular LEA surgery. There was a statistically significant increase in complications with a low SAS after LEA surgery. This is even more pronounced when the TFA sub-group is analyzed separately. Thus, for a TFA patient with a SAS < 7, the odds of a major complication or death are four times larger than for a patient with a SAS \geq 7. ROC analysis confirms the discriminatory power of the SAS approach

Table 2 Pre-operative characteristics

	All patients (n = 170)	TTA patients (n = 70)	TFA patients (n = 100)	P-value
Sex (women/men)	74/96	26/44	48/52	0.21
%	(44/56)	(37/63)	(48/52)	
Age, yrs	74 (12)	72 (12)	76 (12)	0.01
Body mass index	24.5 (6.5)	24.9 (5.3)	24.2 (7.2)	0.47
Cause for amputation				
Diabetes/arteriosclerosis/other	58/105/7	30/36/4	28/69/3	0.03
%	(34/62/4)	(43/51/6)	(28/69/3)	
ASA-groups, 1-2/3-4	25/142	16/54	9/88	0.03
%	(15/84)	(23/77)	(9/88)	
Dementia	20 (12)	6 (9)	14 (14)	0.34
Cardiovascular disease	46 (27)	22 (31)	24 (24)	0.30
Pulmonary disease	30 (18)	12 (17)	18 (18)	1.00
Cerebral apoplexy	40 (24)	11 (16)	29 (29)	0.07
Kidney disease	45 (26)	17 (24)	28 (28)	0.72
Diabetes mellitus	72 (42)	37 (53)	35 (35)	0.02
Diagnosed with cancer	14 (8)	6 (9)	8 (8)	1.00
Transfused preoperatively (patients)	34 (20)	10 (14)	24 (24)	0.17
NSAID or acetylsalicylic acid (yes)	82 (48)	38 (54)	44 (44)	0.21
Clopidogrel (yes)	35 (21)	13 (19)	22 (22)	0.70
Preoperative hemoglobin, g/L (SD)	108 (16.1)	108 (16.1)	106 (16.1)	0.48
Preoperative thrombocytes (SD)	354 (151)	366 (157)	345 (146)	0.46

Values are the mean (SD) and number (%), ASA: American Society of anesthesiologists; TTA: Transtibial amputation; TFA: Transfemoral amputation.

Table 3 Intraoperative characteristics

	All patients (n = 170)	TTA patients (n = 70)	TFA patients (n = 100)	P-value
Bilateral amputation procedure	9 (5)	4 (6)	5 (5)	
Rank of surgeon, resident/consultant %	116/54	45/25	71/29	0.40
	(68/32)	(64/36)	(71/29)	
Duration of surgery, minutes (SD)	81 (23)	85 (26)	79 (20)	0.06
Neuraxial/general anesthesia	121/49	56/14	65/35	0.04
%	(71/29)	(80/20)	(65/35)	
Vasopressor agents during surgery (yes)	106	37 (52)	69 (69)	0.037
Tourniquet use (yes)	49 (29)	35 (50)	11 (11)	< 0.001
Initial heart rate (beats/min) (SD)	85 (16)	84 (15)	85 (17)	0.77
Initial blood pressure (mmHg)	Sys: 131 (21)	Sys: 131 (20)	Sys: 131 (21)	0.83
	Dia: 73 (13)	Dia: 74 (13)	Dia: 73 (12)	0.552
Lowest heart rate (beats/min)	72 (SD: 1.2)	70 (SD: 1.9)	74 (SD: 1.5)	0.13
Lowest mean arterial pressure (mmHg)	64 (SD: 0.9)	65 (SD: 1.4)	64 (SD: 1.1)	0.32
Estimated blood loss (mL), median (IQR)	300 (IQR: 125-475)	248 (IQR: 88-408)	400 (IQR: 231-569)	0.15
Perioperative blood lactate (SD)	1.2 (1.2)	1.0 (0.5)	1.3 (1.5)	0.33
Perioperative acid-base balance (SD)	7.39 (0.01)	7.41 (0.05)	7.38 (0.09)	0.05

TTA: Transtibial amputation; TFA: Transfemoral amputation.

Table 4 Surgical APGAR score complications (%)

	Total (n = 170)	TTA group (n = 70)	TFA group (n = 100)
Death	30 (18)	9 (13)	21 (21)
Bleeding requiring ≥ 4 units of RBC transfusion within 3 d following operation	28 (16)	7 (10)	21 (21)
Sepsis	12 (7)	4 (6)	8 (8)
Acute myocardial infarction/acute heart failure	7 (4)	0 (0)	7 (7)
Acute renal failure	6 (4)	1 (1)	5 (5)
Pneumonia	18 (11)	5 (7)	13 (13)
Stroke	1 (1)	0 (0)	1 (1)
Pulmonary embolism	0 (0)	0 (0)	0 (0)

TTA: Transtibial amputation; TFA: Transfemoral amputation.

Table 5 Logistic regression analysis of surgical APGAR score groups and complications/death

Score	SAS 9-10	SAS 7-8	SAS 5-6	SAS 0-4
All patients (%)	5 (3)	57 (34)	70 (41)	38 (22)
Complications and deaths within SAS group (%)	1 (20)	14 (25)	29 (41)	22 (58)
Odds Ratio between groups (reference SAS 9-10)	(ref.)	OR = 1.30 CI: 0.13-12.64 P = 0.82	OR = 2.83 CI: 0.30-26.64 P = 0.36	OR = 5.50 CI: 0.56-53.99 P = 0.143
Linearity of the model, OR (95%CI), P-value		2.00 (CI: 1.33-3.03) P = 0.001		
Transfemoral procedure, n = 100 (%)	4 (4)	31 (31)	38 (38)	27 (27)
Complications and deaths within SAS group (%)	1 (25)	8 (26)	17 (45)	20 (74)
Odds ratio between groups (reference SAS 9-10)	(ref.)	OR = 1.04 CI: 0.10-11.52 P = 0.97	OR = 2.43 CI: 0.23-25.51 P = 0.46	OR = 8.57 CI: 0.76-96.52 P = 0.08
Linearity of the model, OR (95%CI), P-value		2.61 (CI: 1.52-4.47) P < 0.001		
Transtibial procedure, n = 70 (%)	1 (1)	26 (37)	32 (46)	11 (16)
Complications and deaths within SAS group (%)	0 (0)	6 (23)	12 (38)	2 (18)
Odds Ratio between groups (reference SAS 7-8)	¹	(ref.)	OR = 0.74 CI: 0.13-4.41 P = 0.74	OR = 2.00 CI: 0.63-6.38 P = 0.24
Linearity of the model, OR (95%CI), P-value		1.12 (CI: 0.55-2.29) P = 0.76		

¹Only one TTA in the SAS 9-10 group. SAS 7-8 is therefore used as the reference group. TTA: Transtibial amputation; TFA: Transfemoral amputation.

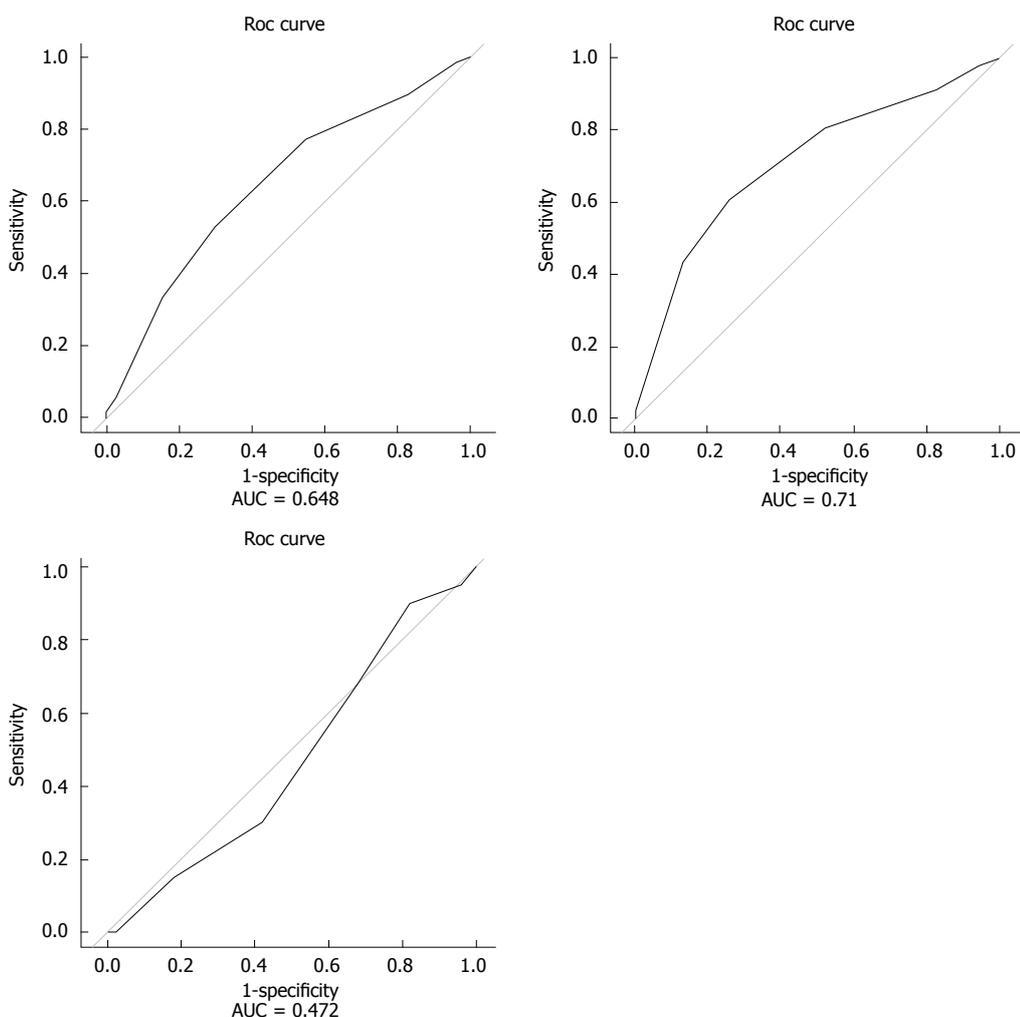


Figure 1 Receiver operating characteristic curve for all patients, transfemoral amputation patients, transtibial amputation patients.

among the TFA patients. However, the SAS model proved to be of no prognostic value in the TTA group.

The population requiring LEA is old, fragile and has several co-morbidities, as clearly shown by this study. When compared to the cohort of general and vascular surgery patients^[1,2,12], our average LEA patient is approximately 20 years older and 84% of patients have an ASA score classifications > 2 (possibly one of the highest reported in any orthopedic cohort), which compares to 34% in the study by Gawande *et al.*^[21]. The mortality rate in the present study is also high, with 18% of patients dead within the first 30 postoperative days. This clearly shows how vulnerable LEA patients are and how an easily applied risk stratification tool would be of great value for individualizing postoperative monitoring and care. Such a score was suggested in 2007^[2,3] and the SAS has proved to be useful in several surgical specialties including gynecologic, urology and colorectal surgery^[1,2,13,14].

However, only recently has the predictive value of the SAS on patients undergoing orthopedic surgery been evaluated^[6,15]. Furthermore, only in spine surgery was the SAS model found to be of value^[6]. Despite these findings, it was expected that the SAS could prove useful in the LEA cohort due to the similarities in demographics shared with patients undergoing general and vascular surgery^[1]. To some extent, the results from this study did confirm our expectations, although it was surprising to see how poorly the score predicted outcome for the TTA patients. In the TFA group, however, approximately four times as many patients with complications were SAS high-risk patients compared to low-risk and the specificity as analyzed by the ROC model confirmed the difference. It is reasonable to conclude that the SAS model has discriminatory power on the TFA sub-group. The TFA group is significantly different from the TTA group in several important variables regarding the SAS model, which increases the risk of postoperative complications or death. For example, TFA patients are significantly older, more often classified as ASA 3-4, more frequently amputated due to severe arteriosclerosis, have procedures more frequently performed under general anesthesia and more frequently require the aid of vasopressor agents such as Ephedrine or Phenylephrine to secure a stable mean arterial pressure compared to TTA patients (Tables 1 and 2). These differences signal that the TTA group is in markedly better pre-operative condition and therefore less exposed to postoperative complications. Another important matter regarding the low specificity of TTA analysis could be superior hemostatic control in the TTA group where 50% had a pneumatic tourniquet applied during surgery. This lower intraoperative blood loss significantly^[16] and potentially reduces the risk of intraoperative tachycardia^[17]. Most acute LEA procedures are performed with a TFA approach^[18], which to some extent is backed by the results from registration of the blood lactate and acid-base balance. Perioperative blood lactate is 0.3 higher in the TFA group with a markedly higher standard deviation

pointing out several high outliers. Furthermore, the blood acid-base balance was found to be lower. In the event of an acute amputation, the operating staff would be challenged to maintain intact vital parameters during surgery. A larger drop in mean arterial pressure or a sudden rise in heart rate or intraoperative bleeding would affect the SAS and the outcome.

Limitations of this cohort study include those associated with its retrospective design and the missing data. Since there are many co-morbidities within this study, there is a risk that some post-operative complications could already have been present before amputation. However, the data collectors within this group have been highly aware of this matter. The study was performed on a unique group of patients often considered poor candidates for intensive care treatment with high post-operative morbidity and mortality. Randomized controlled trials and prospective studies can be a dubious task with this population, and we found the retrospective design sufficient to answer our research question of the study. The study provides some evidence of the value of the SAS in the post-operative treatment. However, further prospective studies examining the performance of the SAS seem warranted.

In conclusion, it seems warranted that the SAS approach provides the medical staff with information regarding the potential postoperative course after TFA surgery, especially when the patients are divided into high- and low-risk groups. The scoring system could prove useful in guiding preventive strategies such as optimizing intraoperative blood pressure or heart rate. The previously established threshold of SAS < 7 to define high-risk patients and SAS ≥ 7 to define low-risk patients was confirmed to be the optimal cut-point by ROC analysis within this study. The SAS showed no discriminatory power in the TTA sub-group, most likely due to optimized hemostatic control, fewer acute amputations and overall better condition compared to TFA patients.

COMMENTS

Background

There is an increasing number of high-risk elderly and severely comorbid patients scheduled for dysvascular lower extremity amputations. An easily applied risk stratification tool would be of great value for individualizing postoperative monitoring and care. The surgical apgar score (SAS, 0-10 points) has a strong correlation with the occurrence of major complications or death within 30-d following general and vascular surgery. However, a similar correlation has not been demonstrated in general orthopedic surgery. The primary aim of this study is to assess whether the SAS is a prognostic tool capable of identifying patients vulnerable to major complications (including death) following lower extremity amputations surgery.

Research frontiers

The authors have reported the first series in the literature of patients with lower extremity amputation who were evaluated with the SAS. The scoring system could prove useful in guiding preventive strategies such as optimizing intraoperative blood pressure or heart rate.

Innovations and breakthroughs

When divided into four groups (SAS: 0-4, 5-6, 7-8 and 9-10), a logistic

regression model shows a significant linear association between decreasing SAS and increasing postoperative complications in transfemoral amputation patients. This effect is even more pronounced when the patients were compared in high-risk and low-risk SAS groups.

Applications

The SAS should be considered during postoperative care of transfemoral amputation patients.

Peer-review

The paper is well-written and this observational study is informative for readers.

REFERENCES

- 1 **Ohlsson H**, Winsö O. Assessment of the Surgical Apgar Score in a Swedish setting. *Acta Anaesthesiol Scand* 2011; **55**: 524-529 [PMID: 21418156 DOI: 10.1111/j.1399-6576.2011.02424.x]
- 2 **Gawande AA**, Kwaan MR, Regenbogen SE, Lipsitz SA, Zinner MJ. An Apgar score for surgery. *J Am Coll Surg* 2007; **204**: 201-208 [PMID: 17254923 DOI: 10.1016/j.jamcollsurg.2006.11.011]
- 3 **Regenbogen SE**, Lancaster RT, Lipsitz SR, Greenberg CC, Hutter MM, Gawande AA. Does the Surgical Apgar Score measure intraoperative performance? *Ann Surg* 2008; **248**: 320-328 [PMID: 18650644 DOI: 10.1097/SLA.0b013e318181c6b1]
- 4 **Haddow JB**, Adwan H, Clark SE, Tayeh S, Antonowicz SS, Jayia P, Chicken DW, Wiggins T, Davenport R, Kaptanis S, Fakhry M, Knowles CH, Elmetwally AS, Geddoa E, Nair MS, Naem I, Adegbola S, Muirhead LJ. Use of the surgical Apgar score to guide postoperative care. *Ann R Coll Surg Engl* 2014; **96**: 352-358 [PMID: 24992418 DOI: 10.1308/003588414X13946184900840]
- 5 **Thorn CC**, Chan M, Sinha N, Harrison RA. Utility of the Surgical Apgar Score in a district general hospital. *World J Surg* 2012; **36**: 1066-1073 [PMID: 22402969 DOI: 10.1007/s00268-012-1495-2]
- 6 **Urrutia J**, Valdes M, Zamora T, Canessa V, Briceno J. Can the Surgical Apgar Score predict morbidity and mortality in general orthopaedic surgery? *Int Orthop* 2012; **36**: 2571-2576 [PMID: 23129225 DOI: 10.1007/s00264-012-1696-1]
- 7 **Dillingham TR**, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J* 2002; **95**: 875-883 [PMID: 12190225]
- 8 **Varma P**, Stineman MG, Dillingham TR. Epidemiology of limb loss. *Phys Med Rehabil Clin N Am* 2014; **25**: 1-8 [PMID: 24287235 DOI: 10.1016/j.pmr.2013.09.001]
- 9 **Kristensen MT**, Holm G, Kirketerp-Møller K, Krashennikoff M, Gebuhr P. Very low survival rates after non-traumatic lower limb amputation in a consecutive series: what to do? *Interact Cardiovasc Thorac Surg* 2012; **14**: 543-547 [PMID: 22298857 DOI: 10.1093/icvts/ivr075]
- 10 **Persson BM**. Sagittal incision for below-knee amputation in ischaemic gangrene. *J Bone Joint Surg Br* 1974; **56**: 110-114
- 11 **Ishii Y**, Matsuda Y. Effect of tourniquet pressure on perioperative blood loss associated with cementless total knee arthroplasty: a prospective, randomized study. *J Arthroplasty* 2005; **20**: 325-330 [PMID: 15809950 DOI: 10.1016/j.arth.2004.10.001]
- 12 **Regenbogen SE**, Ehrenfeld JM, Lipsitz SR, Greenberg CC, Hutter MM, Gawande AA. Utility of the surgical apgar score: validation in 4119 patients. *Arch Surg* 2009; **144**: 30-36; discussion 37 [PMID: 19153322 DOI: 10.1001/archsurg.2008.504]
- 13 **Reynolds PQ**, Sanders NW, Schildcrout JS, Mercaldo ND, St Jacques PJ. Expansion of the surgical Apgar score across all surgical subspecialties as a means to predict postoperative mortality. *Anesthesiology* 2011; **114**: 1305-1312 [PMID: 21502856 DOI: 10.1097/ALN.0b013e318219d734]
- 14 **Haynes AB**, Regenbogen SE, Weiser TG, Lipsitz SR, Dziekan G, Berry WR, Gawande AA. Surgical outcome measurement for a global patient population: validation of the Surgical Apgar Score in 8 countries. *Surgery* 2011; **149**: 519-524 [PMID: 21216419 DOI: 10.1016/j.surg.2010.10.019]
- 15 **Wuerz TH**, Regenbogen SE, Ehrenfeld JM, Malchau H, Rubash HE, Gawande AA, Kent DM. The Surgical Apgar Score in hip and knee arthroplasty. *Clin Orthop Relat Res* 2011; **469**: 1119-1126 [PMID: 21132410 DOI: 10.1007/s11999-010-1721-x]
- 16 **Choksy SA**, Lee Chong P, Smith C, Ireland M, Beard J. A randomised controlled trial of the use of a tourniquet to reduce blood loss during transtibial amputation for peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2006; **31**: 646-650 [PMID: 16750790 DOI: 10.1016/j.ejvs.2006.03.008]
- 17 **Hartmann B**, Junger A, Röhrig R, Klasen J, Jost A, Benson M, Braun H, Fuchs C, Hempelmann G. Intra-operative tachycardia and peri-operative outcome. *Langenbecks Arch Surg* 2003; **388**: 255-260 [PMID: 12920601 DOI: 10.1007/s00423-003-0398-y]
- 18 **Aulivola B**, Hile CN, Hamdan AD, Sheahan MG, Veraldi JR, Skillman JJ, Campbell DR, Scovell SD, LoGerfo FW, Pomposelli FB. Major lower extremity amputation: outcome of a modern series. *Arch Surg* 2004; **139**: 395-399; discussion 399 [PMID: 15078707 DOI: 10.1001/archsurg.139.4.395]

P- Reviewer: Lazzarini PA, Monteiro-Soares M, Turner AP
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Lu YJ



Recurrent missense mutation of *GDF5* (*p.R438L*) causes proximal symphalangism in a British family

Andreas Leonidou, Melita Irving, Simon Holden, Marcos Katchburian

Andreas Leonidou, Marcos Katchburian, Department of Trauma and Orthopaedic Surgery, Maidstone and Tunbridge Wells NHS Trust, Tunbridge Wells TN2 4QJ, United Kingdom

Melita Irving, Department of Clinical Genetics, Guy's and St Thomas' NHS Foundation Trust, London SE1 9RT, United Kingdom

Simon Holden, Department of Clinical Genetics, Addenbrookes Hospital, Cambridge CB2 0QQ, United Kingdom

Author contributions: Leonidou A, Irving M, Holden S and Katchburian M equally made substantial contributions to the conception and design of the paper, acquisition - analysis and interpretation of data; all authors drafted the article and made critical revisions related to the intellectual content of the manuscript and approved the final version of the article to be published.

Informed consent statement: Consent was taken from the patients for their history analysis and genetic testing.

Conflict-of-interest statement: No conflict of interest exists.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Andreas Leonidou, PgDip, MSc, FRCS(Orth), Specialist Registrar, Department of Trauma and Orthopaedic Surgery, Maidstone and Tunbridge Wells NHS Trust, Tonbridge Road, Pembury, Tunbridge Wells TN2 4QJ, United Kingdom. leonidou@doctors.org.uk
Telephone: +44-1892-635986
Fax: +44-1892-634829

Received: January 13, 2016

Peer-review started: January 15, 2016
First decision: March 25, 2016
Revised: August 15, 2016
Accepted: September 21, 2016
Article in press: September 23, 2016
Published online: December 18, 2016

Abstract

Proximal symphalangism (SYM1B) (OMIM 615298) is an autosomal dominant developmental disorder affecting joint fusion. It is characterized by variable fusions of the proximal interphalangeal joints of the hands, typically of the ring and little finger, with the thumb typically being spared. SYM1 is frequently associated with coalition of tarsal bones and conductive hearing loss. Molecular studies have identified two possible genetic aetiologies for this syndrome, *NOG* and *GDF5*. We herein present a British caucasian family with SYM1B caused by a mutation of the *GDF5* gene. A mother and her three children presented to the orthopaedic outpatient department predominantly for feet related problems. All patients had multiple tarsal coalitions and hand involvement in the form of either brachydactyly or symphalangism of the proximal and middle phalanx of the little fingers. Genetic testing in the eldest child and his mother identified a heterozygous missense mutation in *GDF5* c.1313G>T (*p.R438L*), thereby establishing SYM1B as the cause of the orthopaedic problems in this family. There were no mutations identified in the *NOG* gene. This report highlights the importance of thorough history taking, including a three generation family history, and detailed clinical examination of children with fixed planovalgus feet and other family members to detect rare skeletal dysplasia conditions causing pain and deformity, and provides details of the spectrum of problems associated with SYM1B.

Key words: Proximal symphalangism; *GDF5*

© The Author(s) 2016. Published by Baishideng Publishing

Group Inc. All rights reserved.

Core tip: This report highlights the importance of thorough history taking, including a three generation family history, and detailed clinical examination of children with fixed planovalgus feet and other family members to detect rare skeletal dysplasia conditions causing pain and deformity, and provides details of the spectrum of problems associated with SYM1B.

Leonidou A, Irving M, Holden S, Katchburian M. Recurrent missense mutation of *GDF5* (p.R438L) causes proximal symphalangism in a British family. *World J Orthop* 2016; 7(12): 839-842 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/839.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.839>

INTRODUCTION

Proximal symphalangism (SYM1) is an autosomal dominant developmental disorder affecting joint formation^[1]. It is characterized by variable fusions of the proximal interphalangeal joints of the hands, typically of the ring and little finger, with the thumb typically being spared. SYM1 is frequently associated with coalition both of the tarsal bones and the ear ossicles, resulting in conductive hearing loss^[1]. This rare association was first reported by Cushing in 1916 and subsequently by Drinkwater in 1917 for the Brown and Talbot families respectively^[2,3].

Genetic mapping studies have shown that SYM1 shows genetic heterogeneity, with mutations in *NOG*, encoding *NOG*, and *GDF5*, encoding Growth Differentiation Factor 5 (1), causing SYM1A (OMIM 185800) and SYM1B respectively^[4-7].

Here we present a British caucasian family with SYM1B caused by an autosomal dominantly transmitted heterozygous mutation in *GDF5*.

CASE REPORT

A mother presented to our orthopaedic outpatient department with her three children, predominantly for feet related problems. During clinical examination inability to flex the proximal interphalangeal joint of the little fingers was observed and subsequent radiographs revealed symphalangism of the proximal and the middle phalanges. All children and the mother had multiple tarsal coalitions and hand involvement in the form of either brachydactyly or fusion of the proximal interphalangeal joint of the little fingers. The clinical findings of the affected members are demonstrated in Table 1. The father was not clinically affected. The pain and foot deformity significantly impacted upon activities of daily living, limiting exercise capacity and restricting hand use for writing, for example. Hearing was tested and no loss was observed in this family.

DNA sequencing of the eldest son identified a heterozygous missense mutation c.1313G>T in *GDF5*, which

causes the amino acid substitution arginine to leucine at codon 438 (R438L) which predicted to alter *GDF5* signalling and therefore disrupt its function. This was demonstrated to be dominantly transmitted from his affected mother. There were no mutations identified in the *NOG* gene.

DISCUSSION

SYM1 is part of a spectrum of disorders that cause joint fusion. At the most severe end of this spectrum is the multiple synostoses syndrome (SYNS1), which causes severe and widespread joint involvement including the hips, vertebrae and the elbows^[1,8].

Genetic mapping studies have shown that mutations in at least two genes underlie SYM1, *NOG* (SYM1A) and *GDF5* (SYM1B). *NOG* maps to chromosome 17 and encodes the protein Noggin (*NOG*), a bone morphogenic protein (BMP) inhibitor expressed at the sites of joint development^[1]. In the formation of the human skeleton BMPs induce mesenchymal cell proliferation and differentiation into chondroblasts, recruit chondrocytes and promote cartilage formation^[1,9]. *NOG* inhibits cartilage development, leading to separation of the cartilage and thus joint formation^[1,9]. *NOG* mutations lead to under expression of *NOG* resulting in high levels of BMPs, cartilage overgrowth and the absence of joint formation, which affects individuals with SYM1^[1,8-11]. *GDF5* encodes Growth and Differentiation factor 5, a protein belonging to the transforming growth factor beta superfamily which also has an important role in joint development. *GDF5* acts in the same way as BMPs that promote chondrocyte differentiation and cartilage formation^[1,4,5]. The *GDF5* gene is on chromosome 20 and has two coding exons. The c.1313G>T (R438L) mutations in *GDF5* has been previously detected in a family with SYM1^[5] and the causative mechanism is thought to be increased biological activity of *GDF5* leading to joint cartilage overgrowth and subsequent fusion^[1,4,5]. *GDF5* mutations associated with SYM1 and the allelic disorder SYNS1 are summarized in Table 2. The p.Arg438Leu substitution is a gain-of-function mutation known to be associated with proximal symphalangism^[4]. Compared to wild type *GDF5*, the resulting protein shows increased biological activity that alters receptor-binding affinity within the TGFB signalling pathway. Overexpression of *GDF5* disrupts normal joint formation and causes proximal symphalangism.

Hand involvement in patients with SYM1 prevents them from making a fist but does not usually cause significant impairment of functionality required for daily activities^[1]. In the reported family the cause for attendance at the orthopaedic outpatient department was pain and stiffness as a result of tarsal coalitions and fixed planovalgus feet, in general, and not primarily due to hand problems, though restriction was impacting upon their ability to write comfortably. The mother had multiple targeted injections and subsequently developed subtalar joint osteoarthritis and underwent subtalar joint fusion (Figure 1). The other family members have been treated conservatively with orthotics and surgery will be

Table 1 Clinical characteristics of the affected member of the reported family

Affected member (current age)	Hand abnormalities	Tarsal coalition	Conductive hearing loss	Other	Orthopaedic treatment required
Patient 1: Mother (40)	Brachydactyly, no symphalangism	Bilateral: Talonavicular coalition, calcaneocuboid coalition, middle and lateral cuneiform coalition	No	Pituitary adenoma - prolactinoma, platelet storage pool disorder	Yes for painful fixed valgus hindfoot, had targeted injections, developed subtalar osteoarthritis, underwent subtalar fusion Orthotics only
Patient 2: Son (18)	Symphalangism, bilateral little fingers proximal interphalangeal joints fusion ¹	Bilateral: Calcaneocuboid fusion, 3 rd metatarsal - lateral cuneiform, Right talonavicular coalition	No		Orthotics only
Patient 3: Son (15)	Brachydactyly, no symphalangism	Bilateral: Calcaneocuboid coalition, and medial cuneiform to third metatarsal coalition	No	Developmental delay, asthma, under investigation for Marfans	Orthotics only
Patient 4: Daughter (11)	Symphalangism, bilateral little fingers proximal interphalangeal joints fusion ¹	Bilateral: Calcaneocuboid and talonavicular coalition, and medial cuneiform to third metatarsal coalition	No	Developmental delay, asthma, mild platelet dysfunction	Orthotics only

¹For the symphalangism, bilateral little fingers proximal interphalangeal joints fusion of patients 2 and 4, please see the Figure 2.

Table 2 Identified mutations of *GDF5* in relation to proximal symphalangism and multiple synostoses syndrome 2

Ref.	Syndrome	Mutation identified	Effect on codon
Wang <i>et al</i> ^[6]	SYM1	1471 G - A	Glutamic acid to lysine (E491K)
Yang <i>et al</i> ^[7]	SYM1	1118 T - G	Leucine to arginine (L373R)
Seemann <i>et al</i> ^[4]	SYM1	1632 G - T	Arginine to leucine (R438L)
Dawson <i>et al</i> ^[5]	SYNS2	1313 G - T	Arginine to leucine (R438L)

SYM1: Proximal symphalangism; SYNS2: Multiple synostoses syndrome 2.



Figure 1 Radiographs of patient 1 demonstrating multiple tarsal coalitions and right foot radiographs following subtalar joint fusion.

considered at skeletal maturity (Figure 2).

To the authors' knowledge, this is the first report of a British caucasian family with SYM1 associated with a *GDF5* mutation. This case report highlights the importance of taking thorough clinical history and performing detailed clinical examination of patient's

and their affected relatives in establishing a diagnosis in children presenting with fixed planovalgus feet with a view to planning appropriate management. Clinical data from this and other families with SYM1 caused suggest that foot pain is the main medical problem for affected individuals and that hand dysfunction is uncommon



Figure 2 Radiographs of patient 2 (left) and patient 4 (right) demonstrating little fingers symphalangism of proximal a middle phalanx. Patients are unable to flex the proximal interphalangeal joint of their little finger as opposed to the other fingers as demonstrated.

Joint dysfunction can usually be managed by non-operative methods, but may occasionally require surgical intervention.

COMMENTS

Case characteristics

Painful flat feet in a mother and her children.

Clinical diagnosis

Proximal symphalangism.

Laboratory diagnosis

DNA sequencing.

Imaging diagnosis

Radiographs of hands and feet confirming tarsal coalitions and symphalangism.

Treatment

Guided by symptoms and in the form of orthoses, injection therapy and subtalar joint fusion in the mother.

Experiences and lessons

Thorough clinical examination and history taking in order to correctly identify and treat skeletal dysplasias.

Peer-review

This is an interesting case report, highlighting the importance of thorough history

taking. It has great significance to clinical practice, so should be published.

REFERENCES

- 1 **Plett SK**, Berdon WE, Cowles RA, Oklu R, Campbell JB. Cushing proximal symphalangism and the NOG and *GDF5* genes. *Pediatr Radiol* 2008; **38**: 209-215 [PMID: 17994231 DOI: 10.1007/s00247-007-0675-y]
- 2 **Cushing H**. Hereditary Anchylosis of the Proximal Phalan-Geal Joints (Symphalangism). *Genetics* 1916; **1**: 90-106 [PMID: 17245852]
- 3 **Drinkwater H**. Phalangeal Anarthrosis (Synostosis, Ankylosis) transmitted through Fourteen Generations. *Proc R Soc Med* 1917; **10**: 60-68 [PMID: 19979838]
- 4 **Seemann P**, Schwappacher R, Kjaer KW, Krakow D, Lehmann K, Dawson K, Stricker S, Pohl J, Plöger F, Staub E, Nickel J, Sebald W, Knaus P, Mundlos S. Activating and deactivating mutations in the receptor interaction site of *GDF5* cause symphalangism or brachydactyly type A2. *J Clin Invest* 2005; **115**: 2373-2381 [PMID: 16127465 DOI: 10.1172/JCI25118]
- 5 **Dawson K**, Seeman P, Sebald E, King L, Edwards M, Williams J, Mundlos S, Krakow D. *GDF5* is a second locus for multiple-synostosis syndrome. *Am J Hum Genet* 2006; **78**: 708-712 [PMID: 16532400 DOI: 10.1086/503204]
- 6 **Wang X**, Xiao F, Yang Q, Liang B, Tang Z, Jiang L, Zhu Q, Chang W, Jiang J, Jiang C, Ren X, Liu JY, Wang QK, Liu M. A novel mutation in *GDF5* causes autosomal dominant symphalangism in two Chinese families. *Am J Med Genet A* 2006; **140A**: 1846-1853 [PMID: 16892395 DOI: 10.1002/ajmg.a.31372]
- 7 **Yang W**, Cao L, Liu W, Jiang L, Sun M, Zhang D, Wang S, Lo WH, Luo Y, Zhang X. Novel point mutations in *GDF5* associated with two distinct limb malformations in Chinese: brachydactyly type C and proximal symphalangism. *J Hum Genet* 2008; **53**: 368-374 [PMID: 18283415 DOI: 10.1007/s10038-008-0253-7]
- 8 **Potti TA**, Petty EM, Lesperance MM. A comprehensive review of reported heritable noggin-associated syndromes and proposed clinical utility of one broadly inclusive diagnostic term: NOG-related-symphalangism spectrum disorder (NOG-SSD). *Hum Mutat* 2011; **32**: 877-886 [PMID: 21538686 DOI: 10.1002/humu.21515]
- 9 **Marcelino J**, Sciortino CM, Romero MF, Ulatowski LM, Ballock RT, Economides AN, Eimon PM, Harland RM, Warman ML. Human disease-causing NOG missense mutations: effects on noggin secretion, dimer formation, and bone morphogenetic protein binding. *Proc Natl Acad Sci USA* 2001; **98**: 11353-11358 [PMID: 11562478 DOI: 10.1073/pnas.201367598]
- 10 **Athanasakis E**, Biarnes X, Bonati MT, Gasparini P, Faletta F. Identification of a New Mutation (L46P) in the Human NOG Gene in an Italian Patient with Symphalangism Syndrome. *Mol Syndromol* 2012; **3**: 21-24 [PMID: 22855651]
- 11 **Liu F**, Huang Y, Liu L, Liang B, Qu Z, Huang G, Li C, Tian R, Jiang Z, Liu F, Yu X, Huang Y, Liu J, Tang Z. Identification of a novel NOG mutation in a Chinese family with proximal symphalangism. *Clin Chim Acta* 2014; **429**: 129-133 [PMID: 24326127 DOI: 10.1016/j.cca.2013.12.004]

P- Reviewer: Pan F, Reynard LN, Seemann P **S- Editor:** Kong JX
L- Editor: A **E- Editor:** Lu YJ



Glomus tumors of the fingers: Expression of vascular endothelial growth factor

Sittisak Honsawek, Pravit Kitidumrongsook, Pobe Luangjarmekorn, Kawee Pataradool, Voranuch Thanakit, Adisorn Patradul

Sittisak Honsawek, Pravit Kitidumrongsook, Pobe Luangjarmekorn, Kawee Pataradool, Adisorn Patradul, Vinai Parkpian Orthopaedic Research Center, Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society Bangkok 10330, Thailand

Sittisak Honsawek, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Voranuch Thanakit, Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Author contributions: The case was diagnosed by Kitidumrongsook P, Pataradool K, Patradul A; the manuscript was written by Honsawek S, Kitidumrongsook P, Luangjarmekorn P, Pataradool K, Thanakit V, Patradul A; final editing was done by Honsawek S.

Institutional review board statement: N/A.

Informed consent statement: N/A.

Conflict-of-interest statement: All the authors have no conflicts of interests to declare.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Sittisak Honsawek, MD, PhD, Department of Biochemistry and Orthopaedics, Vinai Parkpian Orthopaedic Research Center, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Rama IV road, Patumwan, Bangkok 10330, Thailand. sittisak.h@chula.ac.th
Telephone: +66-2-2564482

Fax: +66-2-2564482

Received: May 10, 2016

Peer-review started: May 12, 2016

First decision: June 4, 2016

Revised: August 27, 2016

Accepted: September 21, 2016

Article in press: September 23, 2016

Published online: December 18, 2016

Abstract

Glomus tumors are uncommon, benign, small neurovascular neoplasms derived from glomus bodies in the reticular dermis. Glomus bodies are found throughout the body to regulate body temperature and skin circulation; however, they are concentrated in the fingers and the sole of the foot. The typical presentation is a solitary nodule in the subungual or periungual area of the distal phalanx. The primary treatment of choice is surgical removal. We investigated expression of vascular endothelial growth factor (VEGF) using immunohistochemistry in glomus tumors of the fingers. All five glomus tumor samples were positive for VEGF expression. VEGF immunoreactivity was largely localized to the cytoplasm of tumor cells, suggesting a contribution of VEGF to the vascularization of glomus tumors.

Key words: Glomus tumors; Fingers; Vascular endothelial growth factor

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Glomus tumors are uncommon, benign, small neurovascular neoplasms derived from glomus bodies in the reticular dermis. The role of vascular endothelial growth factor has never been investigated in glomus tumors of the fingers. This case report demonstrated high

vascular endothelial growth factor (VEGF) expression in the glomus tumors of the fingers, suggesting a contribution of VEGF to the vascularization of glomus tumors.

Honsawek S, Kitidumrongsook P, Luangjarmekorn P, Pataradool K, Thanakit V, Patradul A. Glomus tumors of the fingers: Expression of vascular endothelial growth factor. *World J Orthop* 2016; 7(12): 843-846 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v7/i12/843.htm> DOI: <http://dx.doi.org/10.5312/wjo.v7.i12.843>

INTRODUCTION

Glomus tumor is a relatively rare benign perivascular painful neoplasm arising from the neuromyoarterial structure called a glomus body, a specialized arteriovenous anastomosis involved in thermoregulation^[1]. The diagnosis is virtually relied upon the basis of the clinical history and examination^[2]. The classic clinical triad includes paroxysmal shooting pain, localized tenderness, and hypersensitivity to cold. Patients usually present with a painful, exquisitely tender mass beneath the nail that is accompanied by a faint bluish discoloration. Except for the slight change in color of the nail overlying the tumor, the nail may appear normal. The differential diagnosis includes local infection, osteomyelitis, osteoid osteoma, inclusion cyst, and malignancy.

Vascular endothelial growth factor (VEGF) is a crucial stimulator of blood vessel growth and is one of the most potent growth factors of angiogenesis. Angiogenesis is a fundamental process for growth of new blood vessels from preexisting vasculature during fetal development and tissue repair; however, uncontrolled angiogenesis can contribute to a variety of disorders including neoplastic diseases. In the present study, we performed immunohistochemistry to evaluate the expression of VEGF in glomus tumor tissues.

CASE REPORT

Five patients with solitary glomus tumors of the fingers were surgically treated between 2010 and 2014 at the Department of Orthopaedics of King Chulalongkorn Memorial Hospital, Bangkok, Thailand. The histological diagnoses of each tumor were validated by an experienced pathologist.

The paraffin-embedded tissues were cut in 5 μ m thickness and processed for VEGF staining. Sections were deparaffinized and rehydrated in Tris-buffered saline. Endogenous peroxidase activity was blocked with 0.3% H₂O₂ for 10 min. For antigen retrieval, tissue sections were microwave heated in 10 mmol/L citrate buffer for 5 min. Nonspecific binding was blocked for 20 min with 3% normal horse serum (DAKO, Glostrup, Denmark), followed by incubation with primary antibody (rabbit polyclonal anti-human VEGF antibody 1:100; Santa Cruz Biotech, Santa Cruz, United States) in Tris-buffered

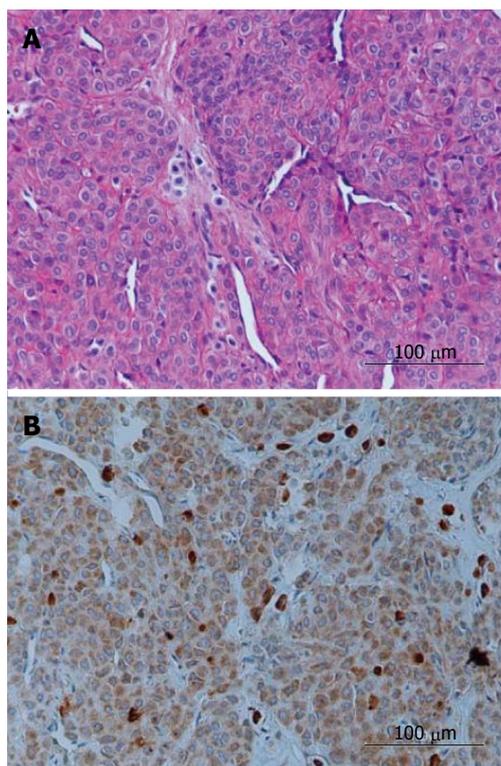


Figure 1 Histopathologic examination. A: The tumor is composed of multiple vascular channels lined by endothelial cells and aggregates of round cells with darkly staining round to ovoid nuclei and eosinophilic cytoplasm (hematoxylin and eosin stain, \times 400); B: The tumour cells are strongly positive for vascular endothelial growth factor (VEGF stain, \times 400). Strong cytoplasmic staining for VEGF in the tumor parenchyma. VEGF: Vascular endothelial growth factor.

saline containing 2% rabbit serum and 1% bovine serum albumin for two hours. Tissues were incubated with the same buffer without the antibody to serve as negative controls. Sections were subsequently stained with biotinylated goat anti-rabbit immunoglobulins (1:400; DAKO) and streptavidin/horseradish peroxidase complex (1:400; DAKO) and incubated at room temperature for 30 min. Reaction products were visualized using diaminobenzidine (Sigma, St. Louis, United States) as the chromogen. The sections were subsequently counterstained with Mayer's hematoxylin and mounted onto microscope slides using a permanent medium.

All five glomus tumor specimens derived from five female patients (age range, thirty-five to forty-eight years) and were located on the fingers. The entire tumors were completely excised surgically.

Representative sections evaluated for histological and VEGF immunostaining are demonstrated in Figure 1, and the grading is present in Table 1. Histopathologic examination demonstrated a well-defined mass to be a glomus tumor, which comprised uniform round or slightly polygonal cells with sharp cellular borders and eosinophilic cytoplasm. The cells are embedded in myxoid and collagenous stroma as solid sheets or thin layer around vascular spaces (Figure 1A). Positive VEGF staining was found in all specimens, with strong VEGF cytoplasmic staining in all five specimens (Figure 1B).

Table 1 Clinical data and scores of vascular endothelial growth factor immunohistological staining

Case	Age (years)	Clinical presentation	Finger	VEGF staining
1	35	Severe pain, point tenderness and bluish discoloration in subungual region	Left thumb	3+
2	38	Episodic pain, cold sensitivity and severe tenderness at the tip of digit	Left middle	2+
3	40	Excruciating pain, numbness and extreme tenderness at the tip of digit	Left small	4+
4	45	Severe pain, worse at night and bluish lesion in subungual base	Right index	2+
5	48	Paroxysmal pain, tingling, paresthesia and point tenderness at the tip of digit	Right ring	3+

VEGF: Vascular endothelial growth factor.

Immunohistochemical examination revealed that the tumor cells are strongly positive for vascular endothelial growth factor. VEGF immunoreactivity was largely localized to the cytoplasm of tumor cells (Figure 1B), suggesting a contribution of VEGF to the vascularization of glomus tumors. The patients' symptoms including severe pain, focal tenderness, and cold hypersensitivity greatly improved and resolved entirely within several weeks following surgical removal. At present, all patients have no pain at rest or at night two years after surgery.

DISCUSSION

Glomus tumors are uncommon, small, painful, and commonly benign hamartomas arising from the arterial end of the glomus body in the reticular dermis. The typical presentation is a solitary nodule in the subungual or periungual area of the distal phalanx. Patients typically present with a triad of symptoms including excruciating paroxysmal pain (worse at night), temperature sensitivity, and severe point tenderness. Direct pressure on the tumor with the head of a straight pin or the tip of a pencil leads to excruciating pain, while pressure applied slightly to one side of it elicits no pain. Immersing the involved hand or digit in cold water or ice cube also result in discomfort.

Glomus tumors usually are less than 1 cm in diameter, often being only a few millimeters in diameter, and may be visible through the overlying tissues as a blue or purple discoloration. They occur more often in the hand nail in 25%-65% of patients. Seventy-five percent are subungual, however, these may pose a difficult diagnosing these tumors^[3]. Although frequently found in the dermis, glomus tumors may occur in deep soft tissue or visceral sites throughout the body including lung, gastrointestinal, and liver^[4,5]. Hypertrophy of a glomus body, an innervated, coiled, arteriovenous dermal shunt that normally controls skin temperature, is evident this tumor. Glomus cells are specialized perivascular muscle cells that are round or oval and have a dense, granular cytoplasm. Nonmyelinated nerve fibers, which are intermixed with thick-walled capillaries, are responsible for the lancinating pain. The mechanism of pain in glomus tumors has not been clearly elucidated, but it may be associated with contraction of myofilaments in response to temperature changes, resulting in an increase in intracapsular pressure^[6]. Although the

precise pathogenesis of glomus tumors is unknown, it is postulated that they either represent hamartomas or reactive hypertrophy secondary to trauma^[6].

Glomangioma and glomangiomyoma are classic variants of the common feature of glomus tumors. The typical histological appearances of the glomus tumors comprise angiocentric uniform sheets of cells with oval nuclei, forming a perivascular collar around vessels. The three different tumor variants are differentiated by their histological characteristics. The common or solid form includes lobules, strands, and broad sheets of rounded, uniform glomus cells with indistinct capillaries in the walls of surrounding large blood vessels. Whereas glomangiomas exhibit prominent vascular structures with dilated veins surrounded by clusters of glomus cells, and glomangiomyomas consisted of prominent vascular and elongated, spindle smooth muscle cells^[7]. In malignant forms, glomangiosarcoma, pleomorphic tumor cells with marked nuclear atypia and frequent mitotic figures are found in variable numbers^[8]. Angiogenesis has been implicated in the progression from benign to malignant tumors. The contribution of angiogenesis and VEGF expression in glomus tumors as yet has not been completely elucidated. It is not yet clear whether there is any difference in VEGF expression between benign and malignant forms of glomus tumors.

In this study, VEGF was detectable in all specimens of glomus tumors. VEGF has been known as a potent angiogenic factor involved in neovascularization. It has been shown that VEGF are expressed in paragangliomas and may contribute to the extreme vascularity of these tumors^[9]. Hence, the elevated VEGF expression in the glomus tumor might play a paracrine role in the angiogenesis that vascularizes around the tumors by capillary sprouting from the adjacent vascular network. Angiogenesis may result in the reconstruction of nutrition for the expanding tumor and could enable further proliferation. However, prospective longitudinal studies with larger sample size are warranted to define the precise role of VEGF in glomus tumors.

These tumors can be removed with the patient under local anesthesia and should be accurately localized by marking the lesion just before operation. Removal of the portion of the nail plate over the area of tenderness and excision of the matrix that appears involved along with a margin of normal-appearing matrix is the treatment of choice. Magnification and high-intensity lighting

facilitate excision of these periungual and subungual masses. Meticulous and complete excision of the usually well-encapsulated lesions is curative, although rates of recurrence 4%-15% have been reported^[10]. Recurrence is attributed to incomplete excision, undetected multiple tumors, or development of a new tumor.

In conclusion, increased VEGF expression was observed in glomus tumors. VEGF could contribute to the process of promoting tumor angiogenesis and might be important in the pathogenesis of glomus tumors.

COMMENTS

Case characteristics

Five female patients (age range, thirty-five to forty-eight years) presented with exquisite pain, point tenderness, cold hypersensitivity on their fingers.

Clinical diagnosis

Severe paroxysmal pain, temperature sensitivity, and severe point tenderness in the finger tips, particularly in the subungual region.

Differential diagnosis

Local infection, osteomyelitis, osteoid osteoma, inclusion cyst, glomus tumor, glomangioma, glomangiomyoma, and malignancy.

Laboratory diagnosis

All labs were within normal limits.

Pathological diagnosis

Glomus tumor.

Treatment

Complete surgical excision of lesion.

Related reports

Glomus tumor is an uncommon benign perivascular painful neoplasm arising from the neuromyoarterial structure of the glomus body. Although frequently found in the dermis, glomus tumors may occur in deep soft tissue or visceral sites throughout the body.

Term explanation

Glomangioma and glomangiomyoma are classic variants of the common feature of glomus tumors. Glomangiomas exhibit prominent vascular structures with dilated veins surrounded by clusters of glomus cells, and glomangiomyomas consisted of prominent vascular and elongated, spindle smooth muscle cells.

Experiences and lessons

The entity of glomus tumor should not be confused with hemangioma or paraganglioma. When making a differential diagnosis of unexplained paroxysmal shooting pain, sensitivity to cold, and localized tenderness in the finger, glomus tumour must be taken into consideration. The standard treatment of choice is surgical removal. Recurrence of glomus tumor generally resulted from incomplete excision.

Peer-review

This is a report of vascular endothelial growth factor in glomus tumors of the fingers. The topic of this manuscript is interesting and it deserves serious consideration for publication. The high VEGF expression in the glomus tumors of the fingers has not been reported in other literatures.

REFERENCES

- 1 **McDermott EM**, Weiss AP. Glomus tumors. *J Hand Surg Am* 2006; **31**: 1397-1400 [PMID: 17027805 DOI: 10.1016/j.jhsa.2006.05.018]
- 2 **Cigna E**, Carlesimo B, Bistoni G, Conte F, Palumbo F, Scuderi N. The value of clinical diagnosis of digital glomus tumors. *Acta Chir Plast* 2008; **50**: 55-58 [PMID: 18807392]
- 3 **Lee JJ**, Park DH, Park MC, Pae NS. Subungual glomus tumours of the hand: diagnosis and outcome of the transungual approach. *J Hand Surg Eur Vol* 2009; **34**: 685-688 [PMID: 19959449 DOI: 10.1177/1753193408104799]
- 4 **Ghigna MR**, Fadel É, Bellini R, Rohnean A, Palazzo L, Dorfmueller P, Dartevelle P, Thomas de Montpréville V. A quite exceptional cause of recurrent hemoptysis. *Chest* 2013; **144**: 1724-1728 [PMID: 24189867 DOI: 10.1378/chest.12-1004]
- 5 **Kihara A**, Fukushima J, Horiuchi H. Glomus tumor of the liver presenting as a cystic lesion. *Pathol Int* 2014; **64**: 295-297 [PMID: 24965114 DOI: 10.1111/pin.12169]
- 6 **Samaniego E**, Crespo A, Sanz A. [Key diagnostic features and treatment of subungual glomus tumor]. *Actas Dermosifiliogr* 2009; **100**: 875-882 [PMID: 20038364]
- 7 **Mravic M**, LaChaud G, Nguyen A, Scott MA, Dry SM, James AW. Clinical and histopathological diagnosis of glomus tumor: an institutional experience of 138 cases. *Int J Surg Pathol* 2015; **23**: 181-188 [PMID: 25614464 DOI: 10.1177/1066896914567330]
- 8 **Park JH**, Oh SH, Yang MH, Kim NI. Glomangiosarcoma of the hand: a case report and review of the literature. *J Dermatol* 2003; **30**: 827-833 [PMID: 14684942]
- 9 **Jyung RW**, LeClair EE, Bernat RA, Kang TS, Ung F, McKenna MJ, Tuan RS. Expression of angiogenic growth factors in paragangliomas. *Laryngoscope* 2000; **110**: 161-167 [PMID: 10646734 DOI: 10.1097/0005537-200001000-00029]
- 10 **Gandhi J**, Yang SS, Hurd J. The anatomic location of digital glomus tumor recurrences. *J Hand Surg Am* 2010; **35**: 986-989 [PMID: 20434277 DOI: 10.1016/j.jhsa.2010.02.019]

P- Reviewer: Ghigna MR, Munoz C, Wang PJ
S- Editor: Qiu S **L- Editor:** A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

